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National Institutes of Health

Dental Research in the United States and Other Countries

Fiscal Year 1979

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Dental Research in the United States and Other Countries

A Catalog of
Dental Research Projects
Sponsored During
Fiscal Year 1979
by Federal and
Non-Federal
Organizations

Prepared Under the
Direction of the
Dental Research
Data Officer,
National Institute of
Dental Research

best copy available

FOREWORD

The National Institute of Dental Research conducts and supports basic, clinical, and applied research and training in the causes, diagnosis, prevention, and cure of oral diseases and disorders.

As part of its broad mission, the Institute is concerned with disseminating research findings and related information to the national and, wherever practicable, the international community of dental practitioners and scientists and to the lay public.

In keeping with this responsibility, this report is published to make timely and comprehensive information available to those who administer, plan, conduct, or use dental research.

David B. Scott

DAVID B. SCOTT, D.D.S.
Director, National Institute of Dental Research

CONTENTS

FOREWORD iii
INTRODUCTION xi

PART 1 DESCRIPTIONS OF RESEARCH PROJECTS

CARIES 1-1

Epidemiology

Identification of Microorganisms 1-1
Distribution and Transmissibility of Microorganisms 1-4
Effect of Salivary Dysfunction on Oral Microorganisms 1-6
General 1-6

Etiology

Tooth Structure and Composition 1-8
Tooth Surface Reactions 1-18
Plaque 1-23
Extracellular Polysaccharides 1-27
Microorganisms 1-31
Salivary Factors 1-43
Diet 1-52
Microbial Fermentation 1-54
Miscellaneous 1-55
Pathology 1-56
Diagnosis and Treatment 1-57

Prevention

Diet 1-59
Salivary Factors 1-60
Cost/Benefit Analysis 1-61
Clinical Trials, General 1-62
Antibacterial 1-63
Antiplaque 1-67
Enamel Sealants and Surface Modifers 1-69
Fluoride, Topical 1-72
Fluoride, Ingested 1-80
Other Trace Minerals 1-87
Immunization 1-89
Hygiene, General 1-94
Motivation 1-94
Demonstration 1-95

PERIODONTAL DISEASE 1-100

Epidemiology 1-100

Etiology

Plaque 1-100

READEX FICHE

Miscellaneous Etiological Factors 1-120
Connective Tissue Structure and Function 1-121

Pathology

Inflammatory Response 1-127
Tissue Destruction and Healing 1-150
Miscellaneous 1-186
Diagnosis and Treatment 1-187

Prevention

Plaque 1-194
Calculus Removal and Mineralization Interference 1-195
Inflammation 1-196
Connective Tissue Metabolism 1-196

SOFT TISSUE DISEASES 1-197

Herpes Simplex Virus Infections

Epidemiology 1-197
Etiology 1-197
Pathology 1-199
Diagnosis and Treatment 1-200
Prevention 1-203

Recurrent Aphthous Ulcers and Other Mucocutaneous Disorders

Epidemiology 1-205
Etiology 1-206
Pathology 1-209
Diagnosis and Treatment 1-209
Prevention 1-209

Tumors of the Oral Mucosa and Connective Tissues

Epidemiology 1-210
Etiology 1-213
Pathology 1-221
Diagnosis and Treatment 1-226
Prevention 1-229

Tumors and Other Diseases of Salivary Glands

Epidemiology 1-230
Etiology 1-233
Pathology 1-237
Diagnosis and Treatment 1-242
Prevention 1-245

Dental Pulp Studies

Etiology 1-246
Pathology 1-247
Diagnosis and Treatment 1-247

CRANIOFACIAL ANOMALIES, GENERAL 1-249

Epidemiology 1-249

Etiology

Developmental Biology 1-249

Genetics 1-258
Embryology 1-260
Craniofacial Growth 1-262
Comparative Sciences 1-266

Pathology

Craniofacial Growth 1-266
Physiology 1-270

Diagnosis and Treatment

Craniofacial Measurement 1-273
Craniofacial Growth 1-275
Growth Promoting Factors 1-277
Physiology 1-278
Osteogenesis 1-280

CLEFT LIP/CLEFT PALATE 1-283

Epidemiology 1-283

Etiology

Craniofacial Growth 1-283
Embryology 1-285
Teratology 1-289
Genetics 1-293

Pathology

Speech 1-295
Craniofacial Growth 1-296
Audiology 1-297
Diagnosis and Treatment 1-297

OTHER CONGENITAL ANOMALIES AND SYNDROMES 1-299

Etiology

Craniofacial Growth 1-299
Teratology 1-299
Genetics 1-300
Pathology 1-301
Diagnosis and Treatment 1-302

MALOCCLUSION 1-304

Etiology

Developmental Biology 1-304
Genetics 1-305
Functional Effects on Morphology 1-306
Craniofacial Growth 1-308

Pathology

Craniofacial Growth 1-309
Physiology 1-310
Speech 1-313

Diagnosis and Treatment

Orthodontic Treatment 1-313
Surgery 1-316
Craniofacial Growth and Remodeling 1-318
Jaw Movement Analysis 1-319
Tooth Attachment and Displacement 1-321

ACQUIRED MALRELATIONS AND ACCIDENT CASES 1-322

Pathology 1-322
Diagnosis and Treatment 1-322

RESTORATIVE MATERIALS AND PROSTHESES 1-324

Diagnosis and Treatment

Restorative Filling Materials 1-324
Bonding Agents 1-334
Prostheses - Facial 1-337
Prostheses - Oral 1-339
Implants 1-345
General Studies 1-355
Endodontics 1-359
Transplants/Replants 1-361
Prevention 1-361

PAIN CONTROL AND BEHAVIORAL STUDIES 1-363

Epidemiology 1-363

Etiology

Basic Neurophysiology, Anatomy and Biochemistry 1-363

Pathology

Pharmacologic Agents 1-381
Oral-Facial Pain Syndromes 1-382

Diagnosis and Treatment

Dental Fear and Anxiety Syndromes 1-383
Other Behavioral Syndromes 1-387
Dental Pain Syndromes 1-389
Oral-Facial Pain Syndromes 1-390
Prevention 1-392

CLINICAL EVALUATIONS 1-392

Equipment/Instruments/Devices 1-392
Drugs 1-393
Materials 1-394
Procedures - Prosthodontic 1-396
Procedures - Radiographic 1-398
Procedures - Surgical 1-400

Procedures - Other Procedures 1-401
Other Clinical Evaluations 1-402

DENTAL ANTHROPOLOGY/FORENSIC DENTISTRY 1-403

DENTAL CARE AND PRACTICE 1-405

DENTAL ECONOMICS 1-409

DENTAL EDUCATION 1-409

Dental Students 1-409
Dentists/Specialty Training 1-410
Dental Auxiliaries 1-410
Dentists/Continuing Education 1-410
Patient Education/Motivation 1-411
Clinical Cancer Education 1-411

DENTAL MANPOWER 1-418

Dentists 1-418
Dental Auxiliaries 1-419

MISCELLANEOUS 1-420

PART II INDEXES

INVESTIGATOR INDEX 2-1

PERFORMING INSTITUTION INDEX 3-1

SUPPORTING AGENCY INDEX 4-1

INTRODUCTION

PURPOSE

Dental Research in the United States and Other Countries, Fiscal Year 1979, attempts to present a comprehensive picture of ongoing dental research in terms of project titles and descriptions, investigators, subject areas, sponsors, performing institutions, and funds. The publication includes all dental research projects registered with the Smithsonian Science Information Exchange, Inc.

COVERAGE

Reporting requirements imposed by Federal sponsors assure that the coverage of U.S.-sponsored research is fairly accurate and complete. Reporting of research projects by non-Federal sponsors and by countries other than the U.S. is strictly voluntary and far from being complete. Industry is particularly reluctant to disclose its research which is probably much greater than the number reported in this issue.

FISCAL YEAR

Because it serves the National Institute of Dental Research (NIDR) as an administrative aide for its own projects, the publication is geared to the U.S. Fiscal Year. Since October of 1976, this is the period of time from October 1 through September 30.

FUNDS

United States' sponsors reported 1,183 dental research projects for an estimated $66 million. In cases where the amount of support was not reported, a calculated average figure was assigned. Since the coverage of countries other than the U.S. is so incomplete and to avoid the problem of international monetary exchange rates, no attempt has been made to develop comparable data for other countries.

FORMAT

This report is divided into two main parts. The first comprises descriptive summaries for 1,319 projects. Of these, 1,183 are sponsored by the U.S. and 136 by other countries. Each summary includes the project title, investigator's name, performing institution, sponsor's project number, sponsor's name, and the actual or estimated amount awarded in FY 1979. The summaries are arranged by chapters which parallel a classification system designed by NIDR for analysis of its dental research effort. NIDR program leaders or the investigators assigned the projects to specific subject areas or chapters. A project that fell into more than one chapter will have a full description in only one with references from the others.

The second part comprises three indexes: an Investigator Index, which lists the principal investigators and associate investigators alphabetically with references to their projects; the Performing Institution Index, which lists the performing institutions alphabetically with references to their projects; and the Supporting Agency Index, which lists the funding organizations alphabetically with references to their projects.

OMISSIONS

Some projects may appear to have been omitted from the publication because the Notice of Research Project form was not received in time to be registered in the SSIE data system or the project period may not have coincided with the U.S. Fiscal Year being published. Other projects will be missing if the dental aspect of the research is not obvious in either the description or the title. A project missing from one chapter may have been placed in another and it will be necessary to find it by means of the indexes. We are truly sorry if we have omitted a project for any reason as we are anxious to have the publication as informative as possible.

ACKNOWLEDGEMENTS

While it is not possible to acknowledge all of those who participated in the completion of this catalog, some of the major sponsors of dental research were called upon to provide additional review and documentation. They were: Dr. Gino C. Battistone of the U.S. Army Institute of Dental Research; Captain James F. Kelly of the U.S. Navy Dental Corps; and Dr. Albert J. Aaronian and Dr. John N. Trodahl of the Veterans Administration.

COMMENTS

Investigators and sponsors of dental research, regardless of country, are urged to report their research to the Dental Research Data Officer, National Institute of Dental Research, National Institutes of Health, Bethesda, Maryland 20205, U.S.A. There is no charge for registration and forms will be sent on request.

Comments in regard to this publication are welcome and should be addressed to the Dental Research Data Officer.

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SSIE NUMBER

NOTICE OF RESEARCH PROJECT

DENTAL RESEARCH

SUPPORTING ORGANIZATION:

SUPPORTING ORGANIZATION NUMBER(S):
Contract No:
and/or
Control No:

PROJECT TITLE:

INVESTIGATOR(S):

DEPARTMENT/SPECIALTY, School or Division

PERFORMING ORGANIZATION:
Name and
Address:
Including
Zip Code.

PERIOD FOR THIS NRP:
Start Date:
End Date:
Annual Funding:

PROJECT SUMMARY: Be brief-200 word maximum: (Include Objective, Approach, Current Plans and/or Progress)

SI-SSIE 79

Dental Research Data Officer
National Institute of Dental Research
National Institutes of Health
Bethesda, Maryland 20205, U.S.A.

DESCRIPTIONS OF RESEARCH PROJECTS

I. CARIES

EPIDEMIOLOGY - IDENTIFICATION OF MICROORGANISMS

1.0001, INVESTIGATE PLAQUE IN MEDELLIN, COLOMBIA, SOUTH AMERICA
G.W. Gillespie, Pan American Health & Education Foundation, *525 23rd St. N.W., Washington, District of Columbia* 20037 (N01DE62457 (CONTRACT))

HEW GOAL: To eliminate dental caries as a major public health service problem by preventing caries.

UTILIZATION OF RESULTS: The data will be used to enhance and broaden the knowledge of the pathogenesis of dental caries.

SCOPE: The offeror proposes to study the children resident in the adjacent Colombian communities of Heliconia and Don Matias, which have widely differing caries experience despite the overall great similaritites in their cultures, socioeconomic status, life style and nutritional habits. Previous studies have shown that such a differing caries experience is not attributable to waterborne fluoride. Specifically, it is proposed to study dental plaque for estimation of the content of Streptococcus mutans, Streptococcus sanguis and lactobacillae as well as the ketohexose and magnesium content and the numbers of dividing cells and cells containing intracellular polysaccharide as well as plaque acid formation. Saliva would be studied with respect to flow, antibacterial activity against S. mutans and S. sanguis and for its content of hexose, calcium, magnesium, phosphorus, iodine and immunoglobulin levels. Water from the two communities would be analyzed for alkalinity, hardness, calcium, magnesium, manganese, iodine and carbonate content, investigated for its influence on plaque formed in human subjects, tested for its effect on polysaccharide formation and its capacity to effect agglutination and adherence of microorganisms and evaluated for its influence on caries activity in rodents. The bulk of the laboratory work is to be carried out at the University of Antiogulia with some portion being subcontracted to laboratories with special skills in carbohydrate or base element analysis.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0002, ROLE OF ORAL MICROORGANISMS IN HUMAN DENTAL CARIES
E.H. Beutner, State University of New York, Health Science Center at Buffalo, School of Medicine, Dept. of Microbiology, *3435 Main St., Buffalo, New York* 14214 (N01DE72410 (CONTRACT))

This project represents Phase I of a two-phase study of the application of fluorescent antibody methods to determination of the etiology of dental caries. In this phase, the contractor will prepare and test fluorescent antibody reagents for fourteen different microorganisms. He will also develop and test the feasibility of methodology, both laboratory and clinical, to be used in the longitudinal study, which will be negotiated as Phase II after the successful completion of Phase I.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0003, CHARACTERIZE AND IDENTIFY PLEOMORPHIC ORAL BACTERIA
R.L. Gherna, American Type Culture Collection, *12301 Parklawn Dr., Rockville, Maryland* 20852 (N01DE92418 (CONTRACT))

The contractor will establish a set of well authenticated strains of various genera of oral microorganisms which will be available for distribution to oral microbiologists; compare results of various common media and methods for assessing the same properties; build a data base describing both authenticated laboratory strains and fresh clinical isolates; and construct and test a probability system for identification of pleomorphic bacteria from the oral cavity.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $109,585

1.0004, CELL-WALL ANTIGENS OF CARIOGENIC STREPTOCOCCI

A.S. Bleiweis, State University System of Florida, University of Florida, School of Agriculture, Dept. of Microbiology & Cell Science, *Gainesville, Florida* 32601 (R01 DE 02901-11)

Streptococcus mutans, etiologic agent of dental caries, is divided into 7 serotypes. We have isolated and characterized antigens possessing determinants for serotypes a, b, c, and e. Also, we have found that several strains induce in rabbits anibodies able to react with human heart-tissue in vitro. Crude wall and membrane preparations from these organisms adsorb tissue-reactive antibodies from human acute rheumatic fever sera. Preliminary data indicate that S. mutans may contain heart-reactive antigens (HRA) in common with S. pyogenes, etiologic agent of rheumatic diseases. These findings warrant caution in the trial of proposed anti-caries vaccines. Presently, we are preparing both purified cell walls and membranes, the latter from mutanolysin-induced spheroplasts of S. mutans, in order to isolate streptococcal HRA's for purification and characterization by immunochemical and immunological means. Also, we shall attempt to determine the ultrastructural localization in human tissue of antibody binding sites. A senstitive technique for immunocytologic staining, horseradish peroxidase, will be employed. The presence of common or distinct binding sites for the anti-streptococcal immunoglobulins (S. mutans vs. S. pyogenes) will be determined. Finally, the possible origin of binding sites will be studied as we attempt to link lipoteichoic acid-HRA complexes to erythrocyte membranes.

BIBLIOGRAPHIC REFERENCES: Antigens of Streptococcus mutans: Isolation of a serotype-specific and a cross-reactive antigen from walls of strain V-100 (serotype e). J.R. Wetherell, Jr. and A.S. Bleiweis. Infect. Immun. 19, 160 (1978). Purification of lipoteichoic acids by using phosphatidyl choline vesicles. L.J. Silvestri, R.A. Craig, L.O. Ingram, E.M. Hoffmann, and A.S. Bleiweis. Infect. Immun. 22, 107 (1978).

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $72,312

1.0005, STREPTOCOCCUS MUTANS - STRAIN TYPING AND INHIBITION

R.A. Kolstad, Baylor College of Dentistry, School of Dentistry, Dept. of Microbiology, *800 Hall St., Dallas, Texas* 75226 (R01 DE 03923-05)

The main goal is to develop a non-cariogenic strain of bacteria, highly capable of colonizing hard surfaces throughout the mouth, which continuously releases toxins which kill S. mutans, which are not activated in vivo, and which are non-toxic to humans.

BIBLIOGRAPHIC REFERENCES: Upton, G. W., Dalton, H. P., Kolstad, R. A.: Bacteriocin typing of streptococcal isolates from endocarditis. J. Clin. Micbiol. 5, 517-520, 1977. Rosen, S., Kolstad, R.A.: Dental caries in gnotobiotic rats inoculated with a strain of Peptostreptococcus intermedius. J. Dent. Res. 56, 187, 1977.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0006, LONGITUDINAL STUDY OF DENTAL ROOT SURFACE CARIES

R.P. Ellen, University of Toronto, Dept. of Clinical Sciences, *92 College St., Toronto, Ontario, Canada* M5S 1B2 (R01 DE 04464-03)

A 3-year longitudinal clinical research project is proposed to study the incidence of root surface caries and the microbial flora associated with the initiation of lesions. The elderly population at Parkwood Hospital, London, Ontario, will be studied. A preliminary study of root caries prevalence in this population indicated that a sufficient number of new lesions should develop.

Each of approximately 50 subjects will be examined annually to record 1) plaque accumulation and periodontal inflammation indices; 2) distribution of developing root lesions; 3) distance of lesions from the crest of gingival margins; and 4) gingival recession. Bitewing radiographs will also be taken.

An average of 8 root plaque samples and a saliva sample will be collected from each subject three times annually. The samples will be diluted and plated on non-selective and selective media. After transportation of plates to Toronto, the proportions and isolation frequency of potentially cariogenic bacteria in the total cultivable flora will be determined, with special reference to Streptococcus mutans, Actinomyces viscosus, Actinomyces naeslundii, lactobacilli, enterococci, and Arthrobacter-like microorganisms.

A bacterial flora profile will be incorporated in the general computer analysis to determine the relationship of the degree of odontopathic infection and the clinical parameters measured. The degree of association of both bacterial and clinical parameters with the initiation of root lesions will be calculated. The data should indicate the microbial and periodontal environments which determine susceptibility to root caries or maintenance of root surface health.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0007, LONGITUDINAL STUDY OF DENTAL ROOT SURFACE CARIES

D.W. Banting, University of Western Ontario, School of Dentistry, Paediatric & Comm Dentistry, *London, Ontario, Canada* (R01 DE 04465-03)

A 3-year longitudinal clinical research project is proposed to study the incidence of root surface caries and the microbial flora associated with the initiation of lesions. The elderly population at Parkwood Hospital, London, Ontario will be studied. A preliminary study of root caries prevalence in this population indicated a high risk of this disease.

Each of approximately 50 subjects will be examined annually to record: 1) plaque accumulation and periodontal inflammation indices; 2) distribution of developing root lesions; 3) distance of lesions from the crest of gingival margins; and 4) gingival recession. Bitewing radiographs will also be taken.

Root surface plaque samples will be collected from each subject three times annually. The samples will be diluted and plated on non-selective and selective media. After transportation of plates to Toronto, the proportions and isolation frequency of potentially cariogenic bacteria in the total cultivable flora will be determined, with special reference to streptococcus mutants, Actinomyces viscosus, Actinomyces naeslundii, lactobacilli, enterococci, and Arthrobacter-like microorganisms.

A bacterial flora profile will be incorporated in the general computer analysis to determine the relationship of the degree of odontopathic infection and the clinical parameters measured. The degree of association of both bacterial and clinical parameters with the initiation of root lesions will be calculated. The data should indicate the microbial and periodontal environments which determine susceptibility to root caries or maintenance of root surface health.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0008, HANDLING OF MICROBIAL STRAIN INFORMATION BY COMPUTERS

M.I. Krichevsky, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Microbial Systematics Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00044-09 ODIR)

For summary: see 2.0025.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$30,710

1.0009, THE EVALUATION OF A MEDIUM FOR THE ISOLATION OF ACTINOMYCES FROM DENTAL PLAQUE

W.A. Little, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00244-03 CPR)

CNAC-20 agar was evaluated as a differential medium for strains of Actinomyces viscosus and Actinomyces naeslundii. Human and monkey plaque specimens, in addition to stock strains of actinomyces and other oral bacteria were cultured on CNAC-20 agar. Plaque isolates were made from colonies judged to be actinomyces or non-actinomyces on the basis of morphology. Verification of these isolates was made with fluorescein labeled antisera specific for A. viscosus and A. naeslundii.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$5,162

I. CARIES

1.0010, ALGORITHMS FOR MICROBIAL SYSTEMATICS

C.A. Walczak, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Microbial Systematics Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00250-02 ODIR)

For summary: see 2.0027.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $13,631

1.0011, FLUORESCENT ANTIBODY METHODS TO DETERMINE THE PREVALENCE OF CERTAIN PLAQUE BACTERIA

L.A. Thomson, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00264-01 CPR)

Several laboratories are collaborating in developing, evaluating, and improving 'reagent grade' fluorescent antibody (FA) conjugates for specific dental plaque bacteria considered important in caries etiology.

These conjugates are being used to determine the prevalence of certain organisms in plaque samples from various locations.

BIBLIOGRAPHIC REFERENCES: Wong, M.C., McKinney, R.M. and Thomson, L.A. Soluble Antigen Extract Used as Blocking Agents to Obtain Specificity in Serotyping of Streptococcus mutans. J. of Immun. Methods, in press, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $28,994

1.0012, A LONGITUDINAL EPIDEMIOLOGICAL STUDY ON DENTAL PLAQUE AND THE DEVELOPMENT OF DENTAL CARIES IN 12-15 YEAR OLD SCHOOL CHILDREN

G.L. Slack, Medical Research Council, Dental Epidemiology Unit, *20 Park Crescent, London W1N 4AL, England, United Kingdom*

The objectives of this investigation are: 1. To study the bacteriological characteristics of approximal dental plaque collected from specific sites of young people at a risk to dental disease. 2. To study the bacteriological characteristics of dental plaque over a period of time in relation to the observed pattern of dental caries. 3. To study the patterns of dental disease in selected populations.

A group of 50 children, randomly selected from a larger study population of over 700, have had bilateral plaque samples collected from the distal surfaces of the upper first premolars three times per year. The differential bacterial composition of these samples is analyzed in the laboratory so that changes in the microbial flora at the target sites can be monitored. By the end of 1977 the study will have been in progress for three and a half years and a total of 1,000 plaque samples examined. Stored bacterial isolates from these samples are identified retrospectively. Preliminary results after two years indicate that no single bacterial species is uniquely associated with the onset of dental caries. These studies are expected to continue until 1981.

SUPPORTED BY

Medical Research Council funds n.a.

EPIDEMIOLOGY - DISTRIBUTION & TRANSMISSIBILITY OF MICROORGANISMS

1.0013, CEMENTAL CARIES AS A DENTAL PROBLEM - MICROBIAL ECOLOGY AND ITS RELATION TO PATHOGENESIS

H.V. Jordan, Forsyth Dental Center, Dept. of Oral Microbiology, *140 Fenway St., Boston, Massachusetts* 02115 (P01 DE 02847-110022)

Studies on the etiology and significance of cemental caries as a dental problem will continue. The project will include laboratory studies on extracted teeth with root surface caries in order to characterize the bacterial flora involved. Representative bacterial isolates will be tested in suitable animal models to determine their pathogenic potential for cemental surfaces.

Studies on the establishment and transmission of S. mutans and Actinomyces will be continued. Colonization patterns will be studied in different animal models including gnotobiotic rats and subhuman primates. In order to detect low numbers of organisms at the early stages of colonization, sensitive selective media will be employed. Priority will be placed on a suitable selective medium for Actinomyces. Comparative pathogenicity of the different species of Actinomyces isolated from the human mouth will be investigated. Transmission patterns of S. mutans and Actinomyces will be studied using bacteriocin production and sensitivity characteristics of the organisms. Possible role of bacteriocins as in vivo regulators of plaque ecology will be investigated.

Feasibility of controlling S. mutans and Actinomyces populations in school children by the use of antibacterial compounds will be studied. Bacteriological studies will be coordinated with observations on caries incidence. Particular emphasis will be placed on tests of efficacy using profiles of significant bacteria.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$81,421

1.0014, THE MICROBIAL COMPOSITION OF DENTAL PLAQUE

M.N. Gilmour, Eastman Dental Center, Dept. of Microbiology, *800 Main St. E., Rochester, New York* 14603 (R01 DE 03378-07)

The objective is to consider the possibility that relationships between members of the dental plaque microflora and caries could result not only from a specific etiologic agent, but also from more than one microorganism (or physiological class of microorganisms) or from disturbance of the balance between physiologic classes present where carious lesions are not formed. The latter was indicated probable in pilot study. Therefore a variety of different flora members are being assessed in interproximal plaques from over sound and incipient lesions and longitudinal clinical assessments are made. In addition to the use of the selective media, isolates from non-selective media are gram-stained and 120/sample are being stored using a newly developed procedure for preservation in liquid nitrogen. These will be available for identification if so warranted from analysis of results from selective media. The latter results are being computerized from multivariate analyses. The appropriateness of both multiple regression and multi-dimensional chi-square procedures will be considered for that purpose.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0015, MATERNAL TRANSMISSION OF STREPTOCOCCUS MUTANS

R.J. Berkowitz, University of Pennsylvania, School of Dental Medicine, Dept. of Orthodontics/Pedodontics, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (R23 DE 05357-01)

A 2-year cross sectional investigation is proposed to study the relationship between maternal transmission of Strep. mutans and primary infection of infants by the organism. The subject population will consist of healthy infants that harbor 6 to 8 primary incisor teeth, and their mothers. The infant subjects will all be patients of the Out Patient Clinic of The Children's Hospital of Philadelphia.

Approximately 300 mother-infant pairs will be evaluated. Saliva samples will be obtained from the mothers and pooled plaque specimens will be simultaneously collected from their infants. The number of C.F.U.'s of Strep. mutans per ml of saliva will be determined for each maternal saliva specimen. In addition, the infant's plaque sample will be evaluated for the presence or absence of the organism.

The resulting data will be utilized in a statistical model that permits testing of the following hypotheses: 1) The mean salivary level of Strep. mutans in a population of mothers whose infants harbor the organism is statistically different than the mean salivary level of Strep. mutans in a population of mothers whose infants do not harbor the organism. 2) There is a statistically significant increase in the frequency of isolation of Strep. mutans from a population of infants whose mothers harbor salivary levels of the organism in excess of 10 to the 5th power cells per ml saliva as compared to the frequency of isolation from infants whose mothers harbor less than 10 to the 5th power cells of the organism per ml saliva.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$38,750

1.0016, STUDIES ON THE CARIOGENIC MICROORGANISM, STREPTOCOCCUS MUTANS

A.H. Rogers, University of Adelaide, School of Dentistry, Dept. of Oral Biology, *Adelaide, S. Australia 5000, Australia* (73/2003)

The main objectives of the project are (a) to determine whether dental caries is a transmissible disease in humans by monitoring the inter-personal transfer of Strep. mutans (b) to isolate, purify and characterize some Strep. mutans bacteriocins and (c) investigate the role of bacteriocins and other factors in modifying the microbial flora in experimental rats. This aspect is being conducted jointly with the Department of Preventive Dentistry, University of Nijmegen, The Netherlands.

Using a bacteriocin typing method developed in our laboratory, it has been shown that transfer of Strep. mutans can occur within families and more extensive studies are in progress.

Studies with non-bacteriocinogenic mutants of Strep. mutans in both germ-free and specific pathogen free (SPF) rats have indicated that bacteriocins play a role in modifying plaque flora, albeit on a micro-ecological scale. Various intracellular glucan (IG)-deficient mutants are being tested in germ-free rats and the results so far indicate that IG plays an important role in the cariogenicity of some strains but not others.

Another factor being investigated is the effect of the resident plaque microflora on the establishment of Strep. mutans in SPF rats. Results so far indicate that the stability of such a flora can have a marked effect on the establishment of this cariogenic organism.

SUPPORTED BY

National Health & Medical Research Council	funds n.a.

EPIDEMIOLOGY - EFFECT OF SALIVARY DYSFUNCTION ON ORAL

MICROORGANISMS

1.0017, ORAL DISEASE IN IMMUNODEFICIENT CHILDREN

T. Lehner, University of London, Guys Hospital Medical School, Dept. of Oral Immunology & Microbiology, *London Bridge, London SE1 9RT, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$13,614

EPIDEMIOLOGY - GENERAL

1.0018, NATIONAL CARIES PREVALENCE SURVEY

T.W. McKenna, Westat Inc., *11600 Nebel St., Rockville, Maryland* 20852 (N01DE92421 (CONTRACT))

Plan and conduct the gathering of data for a survey of the prevlence of dental caries among school aged children in the continental United States. Develop and utilize a probability sample according to NIDR specifications of children in grades Kindergarten through twelve (K-12). Conduct examinations for dental caries, gingivitis, and need for dental treatment on children in randomly selected classrooms; record their residence history; obtain and record the fluoride content of their drinking water; and provide these data to the NIDR. Examinations will be conducted during the 1979-1980 school year.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$1,257,142

1.0019, HOST FACTORS IN CARIES RESISTANCE

I.D. Mandel, Columbia University, School of Dental & Oral Surgery, Dept. of Prev Dentistry, *Broadway & W. 116th St., New York, New York* 10027 (R01 DE 01554-18)

The major objective of the project is to identify the host factors associated with resistance to dental caries. Adults with no history of dental caries, despite environmental challenge, will serve as the focus for comparative studies with matched subjects with high caries activity. Separately collected salivary secretions, pellicle and plaque will be examined in the two groups for factors that can modify: (1) bacterial adherence, growth, and acid production and (2) the ability of the generated acid to produce demineralization. Parameters to be examined will include: (a) direct antibacterial factors, such as SigA antibody levels against specific components of cariogenic bacteria, lysozyme, lactoferrin and lactoperoxidase (amount and antibacterial activity), (b) aggregation potential using laser light to measure rate, (c) amount and nature of acids and bases produced in plaque, employing a recently modified system of liquid column partition chromatography. Salivary factors already identified as differing in the two groups (albumin binding fraction and 'extra' precipitin bands) will be characterized and quantitated in saliva, pellicle and plaque. The concentration of specific phosphoproteins and cationic proteins will be compared and their protective properties assayed in an in vitro system (in collaborative studies).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$144,518

1.0020, STATISTICAL METHODS IN DENTAL RESEARCH

J.L. Fleiss, Columbia University, School of Public Health, Dept. of Biostatistics, *600 W. 168th St., New York, New York* 10032 (R01 DE 04068-05)

It is the purpose of this research project to continue to develop experimental designs and methods of statistical analysis applicable to dental and oral research problems. Many of the designs elaborated in the past have been concerned with therapeutic trials, particularly in the field of dental caries.

We propose to continue to elaborate appropriate designs and analyses for therapeutic trials, particularly in the field of dental caries, but also in the area of oral biology. We expect to devote considerable attention to the appropriateness of the multivariate techniques for certain types of designs handled routinely in the past by analysis of variance models. The emphasis of multivariate analysis is more feasible now than previously, in view of high-speed computer facilities. These methods have definite applications to practical problems in clinical trials in dental caries.

BIBLIOGRAPHIC REFERENCES: Fleiss, J.L. and Shrout, P.E. Approximate interval estimation for a certain intraclass correlation coefficient. Psychometrika, 43:259-262, 1978. Fleiss, J.L. and Shrout, P.E. The effects of measurement errors on some multi-variate procedures. Amer. J. Pub. Hlth., 67:1188-1191, 1977.

SUPPORTED BY	
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$58,313

1.0021, A STUDY OF HOST FACTORS IN CARIES SUSCEPTIBILITY

D.L. Kolakowski, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Behavioral Sciences & Community Health, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 04938-02)

An extended-family study of caries susceptibility among the demes of a descrete, isolated population is proposed. The effects of diet, natural fluoridation and oral hygiene will be rigorously assessed, and the range of population variation in carious lesions will be determined between and within pedigrees. Genetic and environmental contributions to the variance will be estimated by path analysis and major gene affects will be investigated by pedigree analysis. Thus the probable mode of inheritance as well as the magnitude of any host factors will be specificable. The proposed research constitutes a unique opportunity to bring strict genetic control to the study of caries prevalence cross-sectionally.

SUPPORTED BY	
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$40,795

1.0022, AN EVALUATION OF KNUTSON'S FORMULA FOR ESTIMATING AGE-SPECIFIC DMFT

A. Kingman, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Biometry Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00098-06 CPR)

In 1944 Knutson described a formula for estimating age-specific DMFT means from the percent of individuals in the age group having one or more decayed, missing or filled teeth. This formula was evaluated for both different age ranges, and for different allowable maximum percentages using 14 NCP data sets. The method of weighted least squares was used to fit the formula. Results indicate that restrictions of age range, and maximum percent of individuals with one or more DMF teeth, are necessary before applying the formula. It was determined that for K equals 100, and B equals 0.542 the formula could be applied to age groups in the 5-11 year old range which also had not more than 70% of the children with one or more DMFT.

SUPPORTED BY	
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$2,887

1.0023, DECISIVE FACTORS IN RELATION TO CARIES RESISTANCE

O.B. Dirks, Rijksuniversiteit te Utrecht, Dept. of Preventive Dentistry, *Kromme Nievwe Gracht 29, Utrecht, Netherlands*

Resistance to caries is a relative concept, which implies the ability of a person to remain free from caries lesions under environmental conditions that are cariogenic for comparable persons. From Dutch military recruits three groups of persons were selected: all caries-free persons, and a randomly selected control group and persons with DMF greater than or equal to 30.

The following items are studied: nutrition, social, psychological factors, and genetic factors.

SUPPORTED BY	
(No Supporting Organization Reported)	funds n.a.

ETIOLOGY - TOOTH STRUCTURE & COMPOSITION

1.0024, THE INORGANIC COMPOSITION OF ENAMEL, DENTIN AND CEMENTUM IN NORMAL TEETH AND TEETH FROM PERSONS WITH OSTEOGENESIS IMPERFECTA

R.M. Michelich, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160084)

The inorganic composition of enamel and dentin was determined in teeth from normal individuals and in affected teeth from individuals with osteogenesis imperfecta. The percent ash of enamel and dentin in affected teeth from individuals with osteogenesis imperfecta was significantly higher (p less than 0.001) than that of enamel and dentin from normal teeth. The calcium and phosphorus concentrations in teeth from normal individuals and individuals with osteogenesis imperfecta were the same. Cementum isolated mechanically from normal teeth was found to have a lower ash content and a much higher magnesium content than that found in enamel and dentin.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$2,000

1.0025, QUANTITATION OF ENAMEL DEMINERALIZATION MECHANISMS

W.I. Higuchi, University of Michigan, Ann Arbor Campus, School of Pharmacy, Dept. of Pharmaceutical Chemistry, *Ann Arbor, Michigan* 48104 (R01 DE 01830-17)

Our proposed research has been primarily aimed at testing and examining physical models for enamel demineralization and enamel reactions in general with particular emphasis on those situations that bear on the initiation of dental caries and the actions of therapeutic agents for caries. The general theoretical approach involves quantitatively taking into account the effects of all diffusion processes, all chemical equilibria and reactions, and all other physicochemical factors. Thus, in essence, our research approach has been one based on a 'systems engineering' concept. The resulting theoretical relationships for the various models are being examined in detail with experimental demineralization data obtained with both dental enamel and synthetic mineral (especially, hydroxyapatite) under various conditions. Very recent breakthroughs have led to the development of comprehensive model for dental enamel demineralization based upon two dissolution 'sites' for the apatite crystals in the enamel matrix. This model has been totally consistent with virtually all experimental observations including the chemical kinetics data (pH, common ion, foreign ion and fluoride effects), single crystal morphology changes, and gross morphology changes (e.g., zonal dissolution or, clinically, 'white spot' formation). Current efforts are to investigate and apply this model in the evaluation of several foreign ion effects (Sr, Mg, Ti, Zn, Ba, Cd, Pb, Fe, and Sn), dissolution rate inhibitors (alkyl amines, diphosphonates, polymers and polyelectrolytes), and the dissolution rate behavior in EDTA and in bicarbonate solutions.

BIBLIOGRAPHIC REFERENCES: A Possible Second Site for hydroxyapatite Dissolution in Acidic Media, M.B. Fawzi, J.L. Fox, M.G. Dedhiya, W.I. Higuchi and J.J. Hefferren, J. Colloid Interf. Sci. 67, 304 (1978). A New Two-Site Model for Hydroxyapatite Dissolution in Acidic Media, J.L. Fox, W.I. Higuchi, M.B. Fawzi and M.S. Wu, J. Colloid Interf. Sci., 67, 312 (1978).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$96,401

1.0026, TOOTH ENAMEL APATITE AT THE ATOMIC LEVEL

R.A. Young, Georgia Inst. of Technology, Engineering Experiment Station, Applied Physics Branch, *225 North Ave. N.W., Atlanta, Georgia* 30332 (R01 DE 01912-16)

The long term goal is the elucidation of the atomic-level phenomena and mechanisms important to the understanding and ultimate modification of the biological occurrence, function and dysfunction of the apatite portion of dental hard tissue. The differences between dental 'apatite' and stoichiometric hydroxyapatite are recognized as being characteristics with particular biological interest and the studies are therefore focused on them. The principal emphasis in the currently proposed work is on (1) calcium and hydrosyl ion deficiencies (2) the role of chlorine and (3) the effects of minor substituents, all in human tooth enamel. In part (3), first Sr and then one or more of the elements Pb, Na, Mg, Zn, and Mn will be studied. The approach in all three parts involves (1) the determination of some substitution-interaction features in analog systems with fewer parameters, (2) the deduction of plausible models for the structural locations and roles of the ions and vacancies producing the differences from pure hydroapatite, and (3) the selection of the most probable models on the basis of the stringent requirement that they simultaneously account for all known physical and chemical characteristics of the natural material, tooth enamel. Principal tools are x-ray and neutron diffraction, infrared and laser-Raman spectroscopy, and various chemical analysis methods. Particular strength is given to the model assessment and iterative improvement by the use of the powerful new pattern-fitting structure-refinement method applied to x-ray and neutron powder diffraction patterns of tooth enamel.

BIBLIOGRAPHIC REFERENCES: Some Composition Changes in Human Tooth Enamel Resulting from Heating, D.W. Holcomb, P.E. Mackie and R.A. Young, J. Dent. Res., 58 (Special Issue A), 168 (1979). Crystallographic Changes Induced in Human Tooth Enamel by Moderate Heating, P.E. Mackie and R.A. Young, J. Dent. Res., 58 (Special Issue A), 168 (1979).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$135,233

1.0027, ULTRASTRUCTURAL HISTOPATHOLOGY OF HUMAN DENTAL ENAMEL

J.W. Simmelink, Case Western Reserve University, School of Dentistry, Dept. of Oral Biology & Medicine, *2165 Adelbert Rd., Cleveland, Ohio* 44106 (R01 DE 02525-14)

This project is concerned with developing basic information on the ultrastructural morphology and properties of tooth enamel using transmission and scanning electron microscopy, microradiography, as well as other related physical methods. A special feature of the project is the capability of preparing thin sections of etched or fully calcified enamel for transmission electron microscopy from the same areas that are observed by scanning electron microscopy or microradiography. Objective are to obtain a precise and detailed body of information on the relation between structural organization and solubility properties. Three levels of enamel (surface, mid-region, and dentinoenamel junction) will be specifically studied in relation to solubility differences at the enamel crystal level. The development and maturation of the prism border area will be studied, particularly in deciduous as compared to permanent teeth. The correlated microradiographic-electron microscopic study of caries will be continued. Effects of remineralizing solutions, with and without fluoride, on acid etched enamel thin sections will be examined at the ultrastructural level. This project will also extend to study sealant penetration into etched and incipient caries.

BIBLIOGRAPHIC REFERENCES: Simmelink, J.W., and Nygaard, V.K. Effect of low temperature ashing and hydrazine on dentin and enamel. J. Dent. Res. 57: A205, Special Issue A, January, 1978. El-Beheri, S., Simmelink, J.W., and Hawes, R.R. Effect of phosphoric and nitric acid on surface and fissure enamel. J. Dent. Res. 57:A357, Special Issue A, January, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$82,143

1.0028, CELLULAR CONTROL OF MINERALIZATION

D.R. Eisenmann, University of Illinois, Medical Center at Chicago, School of Dentistry, Dept. of Histology, *1853 W. Polk St., Chicago, Illinois* 60680 (R01 DE 03312-06)

Investigations are designed to learn more about the cellular control and transport of mineral ions which become incorporated into developing enamel and defensive mineralization of primary dentin. Maturative ameloblasts of fluorotic rats contain intracellular deposits of crystalline mineral. Injected cobalt causes a temporary reduction or cessation of mineral ion transport into a forming enamel front. These experimental models are used to trace the pathway of mineral ions as they pass from tissue fluids to mineralizing enamel utilizing electron microscopy, histochemistry and electron microscopic autoradiography. Defensive mineralization of rat molar primary dentin is being further analyzed. The enamel-free region of dentin is being examined microradiographically and electron microscopically before and after eruption of the tooth to ascertain the rate and pattern of intratubular mineralization. Microradiography, scanning and transmission electron microscopy are being used to investigate sclerotic and secondary human dentin formation. The claimed protective value of these tissues needs to be assessed, and details of their physiologic and induced patterns of formation elucidated.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,

National Inst. of Dental
Research $0

1.0029, ELABORATION OF GLYCOPROTEINS IN MINERALIZING TISSUES

A. Weinstock, University of California, Los Angeles Campus, School of Dentistry, Dept. of Periodontics, *405 Hilgard Ave., Los Angeles, California* 90024 (R01 DE 03386-09)

The biosynthesis of glycoproteins in mineralizing tissues is to be investigated by light microscope and electron microscope radioautography, immunocytochemistry, biochemical analysis and subcellular fractionation. To this end, rats will receive 3H-fucose, 3H-mannose, 3H-glucosamine, 3H-galactose or 35S-sulfate intravenously. Some animals will receive cycloheximide prior to injection. Incisor teeth and surrounding bone will be processed after fixation, and labeled precursors will be traced in odontoblasts, osteoblasts and ameloblasts. Intracellular sites of uptake, pathways of migration, the mode of discharge and patterns of deposition of glycoproteins into each matrix will be explored. Reduced ameloblasts, dental cuticle, subsurface enamel matrix and the epithelial attachment will also be examined.

Collagen biosynthesis will be traced in osteoblasts of chick embryo calvaria by combined radioautographic and biochemical studies utilizing 3H-proline. The organelle(s) in which procollagen peptides aggregate during transport and secretion will be identified. Other glycoproteins, glycosaminoglycans, and phosphoproteins will be similarly examined. The endoplasmic reticulum, Golgi apparatus and secretory granules of osteoblasts and odontoblasts will be isolated in order to define their roles in the synthesis of collagen and other glycoproteins, as well as to determine kinetics of transport. The intracellular distribution of procollagen will be examined by immunocytochemistry.

Thus, it is hoped to elucidate the steps involved in the elaboration of matrix glycoproteins, and to determine their roles in the development of calcifying matrices.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $73,550

1.0030, CAPILLARY PHENOMENA RELATED TO CARIES SITES

W.J. O'Brien, University of Michigan, Ann Arbor Campus, School of Dentistry, Dept. of Dental Materials, *Ann Arbor, Michigan* 48104 (R01 DE 03480-06)

The research centers around the study of capillary and other interfacial phenomena related to caries prevention. Current research findings indicate the vital role that adhesion has in the caries process. This research makes use of caries research findings to develop coatings for dental enamel that will interfere with the caries process. Previous studies by this investigator indicate that the negative capillary pressure found in saliva at caries sites must be included in research. The research includes studies of adsorption, adhesion and capillary phenomena with systems relevant to the caries process.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0031, SELENIUM METABOLIC EFFECTS AND DENTAL CARIES

T.R. Shearer, Oregon State Higher Education System, University of Oregon Health Sciences Center, School of Dentistry, Dept. of Biochemistry, *611 S.W. Campus Dr., Portland, Oregon* 97201 (R01 DE 03536-07)

The purpose of this research is to understand the mechanism for increases in dental caries observed in man and experimental animals ingesting elevated quantities of the trace mineral selenium. In order to accomplish the above, we will measure the influence of different dosages of inorganic selenium (sodium selenite) and organic selenium (selenomethionine) on the development of experimental dental caries in the white rat. We also plan to measure the levels of selenium in successive layers of enamel from human teeth in order to determine how selenium is taken up into human teeth (i.e. before or after tooth development). Such studies should help to determine the relative significance of selenium in the total susceptibility of enamel to dental caries.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $32,826

1.0032, STUDIES ON THE MOLECULAR BASIS OF DENTAL CARIES

C.F. Schachtele, University of Minnesota, Minneapolis Campus, School of Dentistry, Dept. of Microbiology, *6 Morrill Hall, Minneapolis, Minnesota* 55455 (R01 DE 03654-07)

The overall objective of the proposed research is to gain insight into the mechanisms by which cariogenic bacteria such as Streptococcus mutans can synergistically and antagonistically interact with other bacteria during dental plaque formation. The specific objectives are: (1) to utilize our quantitative in vitro plaque forming assay to analyze factors involved in heterotypic interactions between oral bacteria. Bacteria which readily form plaque on human teeth such as Streptococcus sanguis and certain gram positive rods will be attached to glass vials modified to contain a stable covalently bound layer of polylysine. This initial layer of cells will be used as a base to analyze factors involved in heterotypic attachment of bacteria found in mature plaque. Emphasis will be placed on the conditions for cell preparation and cell surface components involved in adherence; 2. to analyze the interaction and association of the S. mutans dextransucrase with lipids in order to evaluate the role of such molecules in glucan production and sucrose-dependent adherence reactions. Emphasis will be placed on utilizing homogeneous enzyme preparations and phospholipids known to be produced by S. mutans and/or found in human saliva; and 3. to continue evaluation of the association between dextranase-producing oral bacteria and S. mutans. The ability of dextranase-producing bacteria to inhibit or enhance dextran-mediated heterotypic adherence by S. mutans will be evaluated. Plaque samples will be obtained from incipient white spot lesions and control sites on children's teeth and analyzed for the content of S. mutans and specific dextranase-producing bacteria. Emphasis will be placed on careful diagnosis of the sites to be sampled, the method for obtaining plaque and optimization of conditions for bacterial quantitation. The long-term goal is to define interactions involved in regulating the microbial content of plaqe which could be used to develop caries control measures based on selective inhibition of specific cariogenic bacteria.

BIBLIOGRAPHIC REFERENCES: Schachtele, C. F., Harlander, S. K., & Germaine, G. R. (1977) Streptococcus mutans dextransucrase: Isolation and characterization of activities producing water-soluble and water-insoluble glucans. Int. Assoc. Dent. Res. Abstr., 1977, 360. Choih, S., Smith, Q. T., Germaine, G. R. & Schachtele, C. F. (1977) Modification of gland salivary proteins by oral Streptococcus sanguis. Amer. Assoc. Dent. Res. Abstr., 1977, 265.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $68,679

1.0033, PERMEABILITY CHARACTERISTICS OF DENTIN

D.H. Pashley, Medical College of Georgia, School of Dentistry, Dept. of Oral Biology, *1459 Gwinnett St., Augusta, Georgia* 30902 (R01 DE 03780-07)

The proposed work is designed to measure the important membrane coefficients (i.e. permeability coefficients, hydraulic conductances and reflection coefficients) that have previously been measured in dentin in vitro, in vivo, in dog dentin. Further, by simultaneously measuring isotope clearance rates simultaneously from the buccal and lingual surfaces of the same tooth, we will be able to determine the influence of changes in external hydrostatic or osmotic pressures on pulpal pressures and the rate at which substances permeate through dentin to the pulp. We will attempt to estimate pulpal interstitial fluid tracer (or drug) concentrations and the influence of chemical concentration and/or the incorporation of vasoconstrictors with the solute, on those concentrations. The in vivo reflection coefficients of a variety of solutes and solvents of dental interest will be measured before and after dentin surface manipulations.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $86,260

1.0034, ULTRASTRUCTURE OF TOOTH DEVELOPMENT

E.J. Reith, State University System of Florida, University of Florida, School of Medicine, Dept. of Anatomy, *1600 Archer Rd., Box J-266, Gainesville, Florida* 32610 (R01 DE 04059-04)

The research planned in this project proceeds along three lines. 1) One part of this research proposal consists of mapping the location of open versus closed basal ameloblast junctions in the maturation zone of the rat incisor. This will be done by an analysis of serial sections, both cross sections and longitudinal sections, of the rat incisor tooth. 2) The second part of this proposal consists of an analysis of pyroantimonate histochemistry of the maturation zone of the rat incisor. Electron probe x-ray analysis will be performed to establish the nature of the cation being trapped by the pyroantimonate. Attempts will be made to correlte the histochemistry with the results of the serial section analysis of Part 1. 3) Methods will be worked out for the isolation of enriched fractions of differentiated cells (secretory ameloblasts, stratum intermedium, maturation ameloblasts, papillary cells, odontoblasts).

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $31,920

1.0035, ENAMEL APATITES RELATING TO CARIES SUSCEPTIBILITY

R.Z. LeGeros, New York University, School of Dentistry, Dept. of Biochemistry/Dental Materials Science, *421 1st Ave., New York, New York* 10010 (R01 DE 04123-05)

The long term goal of this study is to define the structural and compositional factors relating to the caries susceptibility and resistance of the tooth mineral. (The mineral phase of tooth enamel and dentine is a non-stoichiometric calcium hydroxyapatite, modified by the presence of minor constituents such as CO30, Mg2 ion, HOP40, Na ion). Studies on strucutural factors include: crystallite size and morphology, lattice parameters, internal strain; thermal stability. Studies on compositional factors will focus on the effects of some minor constituents and of some 'trace elements' (suspected of being either cariogenic or cariostatic) on some properties of biological and synthetic apatites.

Biological materials will include dental enamel from teeth of different mammalian species; from human teeth of known ages; from human teeth of known 'trace element' contents obtained from regions of high and low caries incidence; from fluoridated (shark's teeth) and non-fluoridated fish enameloids. Synthetic apatites will be prepared from aqueous systems in the presence of various types and amounts of 'trace elements' or minor constituents. X-ray diffracion, infrared absorption spectroscopy, atomic absorption spectrophotometry, colorimetry, thermo-gravimetry (TGA), and in some cases, transmission (TEM) and scanning (SEM) electron microscopy, will be employed for characterization of the biological and synthetic materials.

BIBLIOGRAPHIC REFERENCES: LeGeros, R.Z., Legros, R., Bonel, G. Types of 'H2O' in human enamel and in precipitated apatites. Calcif. Tiss. Res. 26: 111-118 (1978). LeGeros, R.Z.,Go, P., Suga, S. Fluoride in fish enameloids: x-ray diffraction and spectroscopic studies. J. Dent. Res. 57: A280 (1978).

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $113,645

1.0036, LOCATION AND STRUCTURAL ROLE OF WATER IN TOOTH ENAMEL

P.E. Mackie, Georgia Inst. of Technology, Engineering Experiment Station, *225 North Ave. N.W., Atlanta, Georgia* 30332 (R01 DE 04151-03)

Succinctly stated, the overall objective of the total project is to obtain an understanding of the occurrence, location, binding, variety, changeability and functional role of the 'water' present in human dental enamel in relation to various properties of human teeth. The primary enamel samples to be studied are sound enamel obtained from teeth removed from persons near the two extremes of the human life span. The samples will be investigated by a variety of analytic techniques designed (1) to identify unambiguously and to assay the water in dental enamel, (2) to determine the location, state of binding and accessibility of the water in enamel, (3) to explain the irreversibility of the dehydration-hydration cycle of enamel, and (4) to determine if coupled substitutions, involving water, are related to the observed variations in the Ca/P molar ratios and heating-induced reduction of OH deficiencies in enamel.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0037, COMPARATIVE ULTRASTRUCTURE OF MAMMALIAN AMELOGENESIS

Z. Skobe, Forsyth Dental Center, Dept. of Electron Microscopy/Oral Microbiology, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 04230-05)

The objective of this study is to determine the structure of enamel and the ultrastructure of the cells involved in amelogenesis in several mammals using both scanning and transmission electron microscopes. The purpose of this investigation is to compare enamel formation and enamel structure of mature teeth of man, monkey, cat, and dog in order to provide a basis for evaluating animal model systems and enhance our understanding of enamel structure (the rat is a widely used experimental animal model whose enamel formation and structure has been examined). Differences in enamel structure among these mammals will be noted, particularly if the enamel structure differs from that observed in human teeth. Emphasis will be given to uncovering basic principals of amelogenesis applicable to all enamel systems. Particular attention will be given to determine ameloblast function during enamel deposition in formation of Hunter-Schreger Bands and Lines of Retzius, and the role of papillary cells and their relationship to reduced ameloblasts.

In the investigation of amelogenesis we will use both standard techniques for transmission microscopy and our approach of separating the apical region of the ameloblasts from the nascent enamel so that the enamel-ameloblast interface can be examined in the scanning electron microscope.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$49,705

1.0038, STRONTIUM AND DENTAL CARIES

M.E. Curzon, Eastman Dental Center, Dept. of Caries Research, *800 Main St. E., Rochester, New York* 14603 (R01 DE 04330-05)

The analysis of samples collected in Northwest Ohio (high strontium area) in October, 1978 will continue for as many trace elements as possible.

Transfer of all analytical data to computer cards with cross reference to individual's residence and caries prevalence.

Studies on the effects of strontium on tooth morphology will continue using an animal model.

Further field studies will be carried out in the fall of 1979 to collect more samples for study and analysis. Emphasis will be given to the collection of plaque and studies on plaque activity, inorganic composition and microbial content.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$87,340

1.0039, FLUORIDE-CADMIUM INTERACTION IN DENTAL CARIES

P.D. Whanger, Oregon State Higher Education System, Oregon State University, School of Agriculture, Dept. of Agricultural Chemistry, *35th & Jefferson Sts., Corvallis, Oregon* 97331 (R01 DE 04615-02)

The proposed research will investigate the interaction of fluoride and cadmium, particularly in regard to the development of dental caries. This will be accomplished by presenting various fluoride-cadmium drinking solutions to rats and measuring the effect of cadmium on experimental dental caries and the cariostatic properties of fluoride. We will test if cadmium alters the uptake of fluoride into enamel, and if fluoride affects the deposition of cadmium in the hard and soft tissues of the rat. The proposed research will also test for correlations between the cadmium and fluoride concentrations in human enamel and their relations to dental caries. These studies will show how one environmental factor, cadmium, influences the development of dental caries.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$20,489

1.0040, FLUORIDE-CADMIUM INTERACTION IN DENTAL CARIES

T.R. Shearer, Oregon State Higher Education System, University of Oregon Health Sciences Center, School of Dentistry, Dept. of Biochemistry, *611 S.W. Campus Dr., Portland, Oregon* 97201 (R01 DE 04616-02)

The studies proposed will measure the effect of cadmium on dental caries. Experiments will determine the extent of caries potentiation by developmental and post-developmental cadmium in the rat caries model. Tests will also determine if cadmium reduces the cariostatic effectiveness of fluoride.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$40,508

1.0041, CHEMISTRY OF CALCIUM PHOSPHATES

W.E. Brown, American Dental Assn., Health Foundation, *211 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 05030-03)

Solubility measurements will be continued on octacalcium phosphate and on hydroxyapatite and tooth enamel in the presence of CO2. The uptake of F ions by the surfaces of hydroxyapatite crystals as functions of pH, F concentration and time will be investigated. Studies will be made on the effects of Galvani potentials on the transport of ions through membranes that simulate the to the surface-plaque layer. Laboratory and pilot clinical studies will be made on a new remineralization procedure. Crystal structure analyses will be made on a monomer which expands on polymerization, on an unusual fluoride compound that appears to have promise as a topical fluoridation product, on a strontium phosphate that may be calcium phosphate nucleation analog, and on several calcium phosphate compounds containing other components.

BIBLIOGRAPHIC REFERENCES: Schroeder, L. W.: Mathew, M.: and Brown, W. E., XO4n- Ion Hydration. The Crystal Structure of Mg3(PO4)2.22H2O, J. Phys. Chem. 82, No. 21 (1978).

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $162,736

1.0042, STATOLITH DIFFERENTIATION IN AURELIA (JELLYFISH)

D.B. Spangenberg, Eastern Virginia Medical School, School of Medicine, Dept. of Pathology, *358 Mowbray Arch, Norfolk, Virginia* 23507 (R01 DE 05048-01)

Calcification mechanisms will be studied using the statolith-synthesizing system of Aurelia. Intracellular nucleation vesicles of statocytes will be examined ultrastructurally to determine their site of origin. EM histochemical methods will used to determine the chemical composition of the vesicles. In addition, efforts to decipher the mechanism of calcification of nucleation vesicles will involve the use of radioisotopes of calcium, sulfate, and phosphate.

The effects of phosphate-containing compounds (pyrophosphates, diphosphonates, cyclic AMP) as well as of hormones (thyroxine, PTH, CT, and GH) in statolith synthesis will be determined. Special attention will be paid to the possible roles of these compounds in affecting the uptake of ions, ion transportation in the statocytes and the mineralization of nucleation vesicles.

An investigation of statolith growth in living intact jellyfish will be conducted using time-lapse cinematography.

Information concerning the role of cells in mediating calcification processes, obtained from the jellyfish calcification model, will be applied to problems of calcification in bones and teeth of higher organisms, including man.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0043, MEASUREMENTS OF ENAMEL PERMEABILITY AS RELATED TO CARIES

F. Brudevold, Forsyth Dental Center, Dept. of Chemistry, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 05253-01)

A sensitive method for measuring in vivo permeability of surface enamel will be applied to the maxillary incisors of two groups of children (N greater than or equal to 30) aged 7 to 8 years and 14 to 15 years in order to study possible changes in permeability related to maturation of the teeth. The same method will be used to assess the in vivo demineralization of enamel produced by acids of similar strength as that of citrus fruits or soft drinks, and to monitor subsequent remineralization. Procedures for evaluating in vivo effects on remineralization of fluoride and other agents will be developed. In addition, the protein extracted from the enamel during the period of demineralization and the extractable protein deposited during remineralization will be subjected to amino acid analysis. With the purpose of developing an intraoral cariogenicity test for foodstuffs, the permeability test will also be used to detect the early stage of caries produced in enamel blocks mounted in a full set of dentures.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $107,235

1.0044, QUANTITATIVE STUDIES OF LYSOSOMES IN THE AMELOGENESIS

C.E. Smith, McGill University, Dept. of Anatomy/Oral Biology, *3655 Drummond St., Montreal, Quebec, Canada* H3G 1Y6 (R23 DE 05424-01)

The objective of this study is to learn more about the status of lysosomes in the process of amelogenesis by characterizing morphologically and biochemically the total pool of lysosomes contained within cells of the enamel organ and by investigating if changes occur in the volumetric size or in the levels of enzymatic activities of this pool in the course of amelogenesis. Three correlated experimental approaches are proposed. These include: (1) stereology to obtain data about the volumetric distribution of lysosomes among the various cell layers of the enamel organ at four time periods in amelogenesis corresponding to a proliferative stage, the start of enamel secretion, the finish of enamel secretion, and the period in the maturation stage where the loss of organic material from the developing enamel is maximal; (2) biochemistry to provide information about the gross activity of enzymes contained within the lysosomal pool of the enamel organ at the stage of enamel secretion as compared to the stage enamel maturation; and (3) electron microscopic cytochemistry to give a qualitative assessment of the ultrastructural sites of enzymatic distribution within the lysosomal pool at the stages of enamel secretion and enamel maturation. To facilitate analysis, the rat incisor is suggested as a useful experimental system for this investigation since the entire sequence of developmental steps in amelogenesis are present along the length of this tooth and the rat incisor has been defined precisely enough for reliable and reproducible sampling.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$25,000

1.0045, ELECTRON ION MICROPROBE INORGANIC ELEMENTS IN MINERALIZATION OF DENTIN

D.E. Newbury, U.S. Dept. of Commerce, National Bureau of Standards, *Washington, District of Columbia* 20228 (Y01DE80027 (CONTRACT))

OBJECTIVES AND WORK SCOPE: This project is the study of calcification of dentine in the tooth using mature rat incisors. Concentration ratios of calcium, phosphorus, and magnesium will be measured within various parts of the cell and as it changes through the predentine into the fully calcified dentine. With the CAMECA electron probe, which is only available in this area at the National Bureau of Standards, tissue structure can be seen in sections of the tooth by using backscatter, secondary or transmitted electrons. The same electron beam can then be centered over the structure or area to be analyzed. The x-rays are then analyzed using energy dispersive and wave length dispersive spectrometers. The presence of elements other than Ca, P and Mg will be locked for using the electron generated x-rays. In addition, it is proposed to use the ion probe which uses an ion beam to dislodge atoms, molecules and molecular fragments from a small area of the tooth section.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$28,000

1.0046, STRUCTURAL STUDIES ON COLLAGEN

B.L. Trus, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Protein Chemistry Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00002-29 LB)

For summary: see 2.0076.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$43,519

1.0047, INFRARED AND RAMAN SPECTROSCOPIC STUDIES OF TEETH AND BONES AND RELATED SYNTHETIC COMPOUNDS

B.O. Fowler, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Molecular Structure Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00012-17 LBS)

The main objective is to determine compositional structural details of the inorganic phase in teeth and bones. Infrared and Raman spectroscopy as well as chemical methods are employed in these studies. Methods are devised for the preparation of synthetic calcium apatites having controlled physical properties (crystal size and perfection) and chemical constituents (e.g., hydroxide, fluoride, chloride, carbonate, water and acid phosphate). The vibrational spectra of these apatites and related compounds are assigned and characterized. Isotopically enriched apatite analogs are prepared to facilitate spectral assignments. The spectroscopic assignments and supplemental spectral data (temperature dependency and polarization) are then utilized to establish compositional and structural details of the apatites in question including: the type and geometry of constitutent ions; the site and number of sites occupied by the ions; orientation of ions; chemical bonding and interactions of ions; and semi-quantitative estimations of the constituents present. The results of findings for these controlled apatite systems are then related to the inorganic phase in calcified tissues.

I. CARIES

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $58,119

1.0048, PROTEIN-CRYSTAL RELATIONSHIPS IN MINERALIZED TISSUES

J.D. Termine, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Molecular Structure Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00074-07 LBS)

For summary: see 2.0077.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $69,936

1.0049, CHEMICAL, STRUCTURAL, AND MORPHOLOGICAL STUDIES ON CALCIUM PHOSPHATES

E.D. Eanes, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Molecular Structure Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00088-06 LBS)

The formation and maturation of calcium phosphates prepared from physiological-like solutions is being studied with a variety of ultrastructural and physical-chemical techniques such as electron microscopy, x-ray diffraction, B-E-T surface area methods, and standard analytical chemistry procedures. Topics of current interest include (1) the effect of ionic fluoride, magnesium, and carbonate on physical properties of crystalline apatite such as crystallinity, specific surface area, and particle morphology, and (2) the effect of these ions on the formation, growth, and stability of precursors to the apatite phase.

BIBLIOGRAPHIC REFERENCES: Eanes, E.D., Meyer, J.L.: The influence of fluoride on apatite formation from unstable supersaturated solutions at pH 7.4. J. Dent. Res. 57:617-624, 1978.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $165,668

1.0050, BIOPHYSICAL STUDIES ON THE STRUCTURE OF CONNECTIVE TISSUE

D.A. Torchia, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Protein Chemistry Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00157-05 LB)

For summary: see-2.0079.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $69,010

1.0051, KINETIC AND THERMODYNAMIC CHARACTERIZATION OF CALCIUM PHOSPHATE PRECIPITATION

J.L. Meyer, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Molecular Structure Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00162-03 LBS)

The purpose of this work is to determine the thermodynamic and kinetic factors which regulate the nucleation, crystal growth and maturation of calcium phosphate crystals. This is accomplished by estimating free ionic activities in solution for all species involved in the crystallization process and relating these terms to the observed precipitation steps. A further correlation is then made between the composition of the solution and the solid calcium phosphate phase in equilibrium with it. The effect of crystallization inhibitors on the precipitation of calcium phosphates is also being studied in order to elucidate their mode of action at crystal surfaces. Emphasis is placed upon inhibitors which occur naturally in physiological systems or which are common therapeutic agents.

BIBLIOGRAPHIC REFERENCES: Meyer, J.L. and Eanes, E.D.: A thermodynamic analysis of the secondary transition in the spontaneous precipitation of calcium phosphate. Calcif. Tiss. Res., 25: 209-216, 1978. Eanes, E.D. and Meyer, J.L.: The influence of fluoride on apatite formation from unstable supersaturated solutions at pH 7.4. J. Dent. Res., 57; 617-624, 1978.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $95,441

1.0052, MICROPROBE ANALYSIS OF DEVELOPING RAT ENAMEL

F.S. Casciani, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Molecular Structure Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00251-02 LBS)

The objectives of this study are the identification and characterization of the inorganic phosphate and carbonate phases and the organic matrix of rodent incisor enamel, and changes in these components which occur during mineralization and maturation. Inorganic and organic phosphate and carbonate phases localized in the tissue during development are analyzed using spectroscopic microprobe techniques. The Raman microprobe, capable of identifying molecular species, and elemental microprobe analyses (X-ray microanalysis and ion microprobe analysis) used in conjunction allow the correlation of data obtained from these two types of complementary analyses. This data then, may be interpreted to discern the distribution patterns of calcium, phosphate, magnesium carbonate and other ions at mineralizing sites in developing enamel.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$54,591

1.0053, SCANNING ELECTRON MICROSCOPE STUDY OF CUSPAL ENAMEL IN DECIDUOUS MOLARS

R.B. Paulson, Ohio State University, Columbus Campus, School of Dentistry, *190 N. Oval Dr., Columbus, Ohio* 43210

The developing cuspal enamel of deciduous molars from 5-6 month old human fetuses was studied with the SEM in order to further elucidate the three-dimensional arrangement of enamel rods directly above the cuspal dentin cone. Incompletely mineralized, prematurely erupted and extracted first deciduous molar cusps from a three month old child, were also studied in a fractured plane and correlations were attempted between the surface view of the forming enamel matrix over the cusp tip close to the dej, and the corresponding area in a fractured plane of the partially mineralized molar. Molar tooth buds were dissected and fixed in 4% glutaraldehyde, osmicated, dehydrated for critical point drying, and carbon and gold coated for SEM viewing in a whole state. The extracted molar teeth were similarly treated, subsequently fractured and EDTA etched. The surface view of the developing cusp around the central axis consists of an area of oversize, up to 10 microns wide rod spaces, separated by 2-3 microns wide interprismatic substance bands. Elevated ridges, 8-10 rod spaces apart, emanate from this central core and run in a cervical direction. Rod spaces on the ridge are smaller and in closer approximation to each other than in the depressed area between the ridges. The corresponding area of the mineralized, fractured molar cusp reveals a 5-10 microns wide hypomineralized layer of enamel adjacent to the dej, wide interprismatic bands and enamel rods and in addition 'Fibrous' extentions emanating from the dentin surface of the dej, bridging the hypomineralized area and extending 20-25 microns into the enamel thickness.

SUPPORTED BY

Ohio State University	funds n.a.

1.0054, ELECTRON MICROPROBE ANALYSIS OF PRE- AND POSTNATAL MINERALIZED HUMAN ENAMEL

U. Kirchner, Freie Universitat Berlin, Inst. fur Klinisch Theoretische Zahn Mund & Kieferheilkunde, *Assmannshauserstrasse 4-6, 1000 Berlin 33, Federal Republic of Germany*

Previous studies led to the assumption that postnatal enamel is better mineralized than the prenatal part. However, due to the applied methods only few sufficient data exist on the degree of mineralization of the different enamel regions. Nevertheless the hypothesis has been developed to explain the origin of the circular caries of deciduous teeth.

Undecalcified longitudinal ground sections were investigated by using wavelength-dispersive microanalysis. Spot analysis and line scans have been made to determine the relative distribution of Ca and P in relation to the microscopic structure. More than 5,000 minute areas of about 30 square microns in cervical, central and incisal regions have been explored.

The results of the study gave no indication that there are significant differences in the degree of mineralization of the pre- and postnatal formed enamel.

SUPPORTED BY

Freie Universitat Berlin	funds n.a.

1.0055, THE STRUCTURE AND THE PHYSICAL AND CHEMICAL PROPERTIES OF NORMAL AND DISEASED ENAMEL

Unknown, Medical Research Council, Dental Unit, *Bristol, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$82,307

1.0056, RELATIONSHIP BETWEEN HISTOLOGICAL APPEARANCE AND COMPOSITION OF THE ENAMEL ORGAN AND ASSOCIATED DEVELOPING ENAMEL

C. Robinson, University of Leeds, Dept. of Oral Biology, *Woodhouse Ln., Leeds LS2 9JT, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$13,273

1.0057, AMINO ACID ANALYSIS OF PROTEIN SAMPLES FROM DENTAL HARD TISSUES

C. Robinson, University of Leeds, Dept. of Oral Biology, *Woodhouse Ln., Leeds LS2 9JT, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$22,690

1.0058, ULTRASTRUCTURAL AND MICROANALYTICAL STUDIES OF THE MECHANISMS OF ORAL DISEASE AND OF THEIR PREVENTION AND TREATMENT

N.W. Johnson, University of London, London Hospital Medical College, Dept. of Oral Pathology, *Turner St., London E1 2AD, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$6,807

1.0059, VARIATION IN ENAMEL SURFACE STRUCTURE

D.K. Whittaker, University of Wales, Welsh National School of Medicine, School of Dentistry, Dept. of Oral Biology, *Heath Park, Cardiff CF4 4XN, Wales, United Kingdom* (31288)

To establish the surface structure of human dental enamel and to investigate its variation in relation to (a) deciduous and permanent teeth (b) tooth type, e.g. incisor, premolar and molar (c) the surface of the tooth e.g. mesial or buccal, (d) the age of the tooth post eruption, (e) the environment of the tooth during its development, e.g. optimum level of fluoride ion. The general purpose of the investigation is to provide basic structural information to allow a less speculative interpretation to be made of both clinical and laboratory research. Those areas in which it might be expected to provide assistance are (a) clinical research, 1. caries incidence, 2. caries resistance studies, 3. preventive techniques, 4. bonded resins, (b) laboratory research. 1. plaque attachment studies, 2. studies of artificial caries, 3. in vitro studies of bonded resin attachment. Scanning electron microscopy following embedding, sectioning and etching will be used as the main technique and some 4000 sectioned surfaces will be examined from up to 500 teeth.

SUPPORTED BY

University of Wales	funds n.a.

ETIOLOGY - TOOTH SURFACE REACTIONS

1.0060, BIOLOGICAL EFFECTS OF ACID ETCHING ON NATURAL TEETH

E.L. Liatukas, Howard University, Graduate School, *2400 6th St. N.W., Washington, District of Columbia* 20001 (S06 RR 08016-090014)

This project is part of a broader program (RR 08016-09) whose summary states: A renewal application is made for continued minority Biomedical support for the Biomedical Interdisciplinary Project at Howard University. It consists of individual research elements with biomedical relevance and requests for support of strong undergraduate and graduate student research participation. The subject areas of Botany, Chemistry, Dentistry, Immunology, Psychology and Zoology are represented among 19 research project elements organized by individual faculty members or collaboratively among faculty in two or more disciplines.

Support is requested for visiting scientists to serve as a part of a Seminar-Science Conference component designed to promote University-wide communication among faculty and student scientists at Howard.

Overall, a program is proposed which will ultimately increase the biomedical research potential at Howard and add to the pool of minorities trained and prepared to perform at a high level in biomedical research.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, Div. of Research Resources	funds n.a.

1.0061, STRONTIUM, LITHIUM, & FLUORINE EFFECT ON DENTAL PLAQUE

M.E. Curzon, Eastman Dental Center, *800 Main St. E., Rochester, New York* 14603 (N01DE72409 (CONTRACT))

Determine the in vitro effects of various levels of strontium, lithium, and fluorine, both singly and in combination, on the physicochemical, microbiological, and biochemical parameters which are known or thought to contribute significantly to dental plaque formation and activity: adsorption of salivary proteins to hydroxyapatite; sorption of bacteria to hydroxyapatite; bacterial saccharides; bacterial agregation; and synthesis and breakdown of extracellular polysaccharides. Also, determine the prenatal, preeruptive, and posteruptive effects of various levels of strontium, lithium, and fluorine on plaque formation and caries development in the rat.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$106,220

1.0062, CRYSTAL STRUCTURES OF CALCIUM AND PHOSPHATE COMPLEXES AND OF RELATED PROTEINS

C.E. Bugg, University of Alabama in Birmingham, School of Dentistry, Dept. of Biochemistry, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130001)

This research program is currently concentrated in two major areas:

Structural studies of calcium and phosphate complexes of carbohydrates, lipids, amino acids, peptides, and proteins. The major objective of these studies is to produce fundamental structural data concerning the factors that control mineral interactions with organic matrices. A secondary objective of these studies is to clarify the types of interactions that are likely to be involved in the transport of calcium and phosphate ions in biological systems, and the roles that calcium ions play in biological agglutination and adhesion processes.

Protein crystallography, with particular emphasis on structural studies of proteins that bind carbohydrates, proteins that interact with cell surfaces, and proteins that are involved in or affect metal and ion transport through cellular membranes. The overall primary objectives of these studies are to obtain fundamental structural data relating to the general properties of cell surfaces and cellular membranes, and to identify those structural properties that control cellular interactions with extracellular matrices and the structural factors that are important in metal and ion transport processes.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$152,681

1.0063, INVESTIGATION OF THE MECHANISM OF PRODUCTION OF CARIOUS LESIONS

T. Koulourides, University of Alabama in Birmingham, School of Dentistry, Institute of Dental Research, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130014)

The intraoral caries test (ICT) model is employed to evaluate the effects of diet, fluorides, various phosphates and phosphonates in the development of carious lesions. The erosive action of certain acid drinks on enamel will be studied. A synthetic saliva substitute will also be studied in patients with xerostomia.

Evaluation of various molecular species as they influence the demineralization-remineralization activities in vitro and in the ICT will continue. Next year efforts will be directed toward elucidating the effect of surface-active agents such as the pyrophosphates, trimetaphosphates, and diphosphonates on the mineral exchange between enamel and its environment, ICT, dental plaques, and saliva.

Assessment of the cariogenic potential of foods, food combinations, and the effect of food additives such as calcium and phosphate salts will continue.

Investigation of the degree of enamel resistance developed after interaction with microbial plaques and selected fluid environments will continue.

Studies of clinical effectiveness of artificial saliva with various levels of fluoride will continue.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$155,434

1.0064, TRANSPORT IN ENAMEL & SOLUBILITY OF FLUORIDATED APATITE

E.C. Moreno, Forsyth Dental Center, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 03187-08)

The purpose of the proposed work is to study the physico-chemical aspects of the processes involved in demineralization and remineralization of dental enamel. Special emphasis will be given to the properties of the tooth-saliva interface. Under natural conditions, part of this interface is the acquired tooth pellicle which forms through a selective adsorption of salivary glycoproteins and peptides. The proposed work encompasses studies on adsorption of purified salivary components to ascertain the way in which the acquired pellicle is built up. The properties of these pellicles will be studied particularly in relation to transport phenomena (e.g. ionic permselectivity) and their effects upon demineralization by acid buffers and cariogenic microorganisms. Studies are also proposed to ascertain the factors controlling enamel remineralization. In this connection, experiments will be conducted to determine the rate of crystal growth of calcium apatites in the presence of salivary components. The results of these experiments will be applied to the study of enamel remineralization in vitro.

BIBLIOGRAPHIC REFERENCES: Adsorption of Amino Acids onto Hydroxyapatite. Kresak, M., Moreno, E.C., Zahradnik, R.T., and Hay, D.I. J. Colloid Interf. Sci. 59, 283-292 (1977). Progressive Stages of Subsurface Demineralization of Human Tooth Enamel. Zahradnik, R. T. and Moreno, E.C. Archs oral Biol. 22, 585-591 (1977).

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $184,002

1.0065, THE KINETICS OF MINERALIZATION OF TEETH

G.H. Nancollas, State University of New York, Buffalo Campus, School of Natural Sciences & Mathematics, Dept. of Chemistry, *3435 Main St., Buffalo, New York* 14214 (R01 DE 03223-09)

The overall objective of the proposed research is the characterization of the kinetics of mineralization of calcium phosphates and inorganic and organic components of teeth such as whole and carious enamel and dentine, predentine, plaque, calculus, unerupted teeth and organic phases such as collagen and elastin. The highly reproducible seeded growth procedure developed in our laboratory will be used over range of ionic strength,concentration and pH typical of those in the mouth. Emphasis will be placed on the use of our new constant composition method which enables the mineralizing phases to be characterized and the rates of reaction to be measured with a precision hitherto unattainable. Thus, this work can now be extended to the kinetic and microscopic monitoring of the surfaces of enamel blocks (both whole and carious) during mineralizaton. The effects ofpotential anti-caries and anti-calculus agents and salivary components in modifying the course of the mineralization will be investigated. In parallel with these studies, solid mineralized phases will be characterized by electron and ion microscopy, x-ray diffraction, surface area determination etc., The kinetics of dissolution of sound and white-spot enamel will be studied using the well-defined hydrodynamics of the rotating disc to provide a model for in vivo tooth surface and sub-surface erosion. Direct measurements will be made of the adsorption and desorption of anti-calculus and anti-caries agents during both re-and de-mineralizaton to relate with the results of the kinetic experiments. The use of the constant composition method in providing kinetic information for the development of possible methods for the remineralization of damaged enamel in the mouth will be of particular interest.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $66,958

1.0066, INTERFACIAL PROPERTIES OF APATITE AND TOOTH MATERIALS

D.W. Fuerstenau, University of California, Berkeley Campus, School of Engineering, Dept. of Materials Sci & Minerals Engin, *Berkeley, California* 94720 (R01 DE 03708-06)

The objectives of this research program are to continue and extend the ongoing investigations on the surface properties of hydroxyapatite, with special reference being given to the elucidation of the mechanism of interaction of fluoride and constituents of salivary proteins with hydroxyapatite have revealed some results which may have far reaching consequences. It is proposed to explore the adsorption of fluoride on HA from aqueous media more thoroughly through the systematic control of a number of solution variables. A study of fluoride adsorption on dental fillers is also contemplated. Direct evidence for distinguishing between chemisorbed fluoride and the formation of fluorapatite or fluorite at the hydroxyapatite surface will be sought through the techniques of electron spectroscopy for chemical analysis (ESCA) and far infrared analysis. In view of the importance of salivary glycoproteins in plaque-development, it is planned to continue our ongoing work on the adsorption of amino acid constituents of saliva on hydroxyapatite and to initiate research on the interaction of surface-active compounds which possess antimicrobial properties (e.g., chlorhexidine) with amino acid-coated hydroxyapatite. We plan to continue our current investigations on the measurement of thickness of thin protein films on fluorite and fluorapatite and also to determine the influence of adsorbed components of tobacco smoke on the dissolution of hydroxyapatite in saliva and fluoride solutions.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0067, MECHANISM OF DENTAL CARIES

W.E. Brown, American Dental Assn., Health Foundation, Research Unit, *211 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 04385-04)

Tooth enamel is subjected to a wide variety of natural and clinical conditions that induce chemical changes in its mineral, but very little is known about the response of the aqueous solution within the enamel to changes in the external variables. We propose to study changes in the compositions of the internal solution as functions of time, depth within the tooth (or within a lesion), composition of the external solution, permselectivity of the tooth surface, and degree of mineralization. The objectives are to learn more about the crucial events that occur within the tooth during caries formation, topical fluoridation, etching of the surface, artificial remineralization, or treatment to dissolve the mineral in dental calculus. The objective is to improve preventive methods and clinical procedures.

A tooth section about 750 microns thickness is cemented between two plastic slides leaving the natural surface of the tooth exposed at the edge. Small wells are drilled through the top slide into the enamel at various distances from the edge. The assembly is placed on the surface of the test solution. Evaporation is prevented by a layer of mineral oil on the top. Micro electrodes are inserted into the solutions within the wells to measure activities of ions, or galvanic potential differences between wells or between a given well and the external solution. Samples removed from the wells are analyzed for calcium, phosphate, fluoride or other ions by ultramicroanalytical techniques that have been developed for this purpose.

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Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $79,301

1.0068, MINERAL-ORGANIC INTERACTIONS IN THE ORAL MILIEU

I. Pullman, New York Medical College, Manhattan Campus, School of Medicine, Dept. of Radiology, *1249 5th Ave., New York, New York* 10029 (R01 DE 04469-01A1)

This proposal addresses itself to two aspects of oral biochemistry. The first concerns the interaction between the enamel surface and the macromolecular components of saliva so as to gain fundamental insight into the formation of the organic pellicle of tooth. The second seeks to initiate an exploration of the molecular basis of bacterial adhesion to tooth surfaces. Electron spin resonance spectroscopy (ESR), having been shown to be especially appropriate to such interface studies, will be the major methodology. Its application will focus on the analysis of materials that have undergone spin-labeling procedures such as the production of free radicals by x-rays or ultraviolet radiation, the binding of transition-ion probes, and the reaction with stable nitroxide radicals.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0069, HYDROXYAPATITE REMINERALIZATION - THE ROLE OF FLUORIDE

J.L. Fox, University of Michigan, Ann Arbor Campus, School of Pharmacy, *Ann Arbor, Michigan* 48104 (R01 DE 04600-03)

A physical model involving two different crystalline sites for dissolution has been developed to explain the kinetics of demineralization and remineralization of hydroxyapatite and tooth enamel. The goals of this project include correlation of the degree of demineralization of HAP crystal slurries and the sites from which it occurred to the degree of subsequent remineralization attainable with fluoride containing remineralizing solutions. In addition the kinetic properties of the dissolution sites both before and after a demineralization/remineralization treatment will be assessed. Finally, a physical model developed from these findings will be the basis for computer simulations of cycles of demineralization/remineralization of HAP pellets followed by various types of acidic attack. Results of computer simulations will be compared with experimentally accessible parameters, such as gradients of fluoride content and mineral density.

The successful completion of this project would lead to greater understanding of the response of teeth to regular fluctuations in saliva composition, and would set the stage for the rational design of therapy for enhancing caries resistance.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $47,060

1.0070, PREVENTION OF DENTAL CARIES

W.E. Brown, American Dental Assn., Health Foundation, *211 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 05354-02)

Etching of enamel surfaces: Improvements in etching procedures will be sought which will reduce the loss of mineral. Special emphasis will be placed on procedures for incorporating fluoride into the tooth in the form of fluorapatite.

Topical fluoridation procedures: Further studies will be carried out to improve procedures which involve formation of CaHPO4.2H2O in the tooth by a pretreatment, followed by a fluoride solution which converts the CaHPO4.2H2O into fluorapatite. Emphasis will be placed on testing of new modalities of application. Animal studies will continue and preliminary clinical studies will be initiated.

Mechanism of fluoride cariostasis: Improvements will be made in the diffusion cell used to study the dynamics of diffusion so that steady state will be attained more rapidly. The effects of neutral salts on the composition of the solution within the 'caries' compartment will be studied.

Role of octacalcium phosphate in tooth formation: Radioactive phosphorus will be used in an effort to study the involvement of octacalcium phosphate in enamel mineral formation.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $149,659

1.0071, MINERAL-ORGANIC INTERACTIONS IN THE ORAL MILIEU

I. Pullman, New York University, School of Dentistry, Dept. of Dental Materials Science, *421 1st Ave., New York, New York* 10010 (R01 DE 05518-01)

This proposal addresses itself to two aspects of oral biochemistry. The first concerns the interaction between the enamel surface and the macromolecular components of saliva so as to gain fundamental insight into the formation of the organic pellicle of tooth. The second seeks to initiate an exploration of the molecular basis of bacterial adhesion to tooth surfaces. Electron spin resonance spectroscopy (ESR), having been shown to be especially appropriate to such interface studies, will be the major methodology. Its application will focus on the analysis of materials that have undergone spin-labeling procedures such as the production of free radicals by x-rays or ultraviolet radiation, the binding of transition-ion probes, and the reaction with stable nitroxide radicals.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $126,030

1.0072, EFFECTS OF POTENTIAL THERAPEUTIC AGENTS ON THE FORMATION AND ACTIVITY OF DENTAL PLAQUE

C. McGaughey, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *5901 E. 7th St., Long Beach, California* 90822 (600-001-P)

Investigations of chemical interactions between polyphosphates and phosphonates (potential anticaries agents) and hydroxyapatite (HA) powder are continuing. All compounds solubilized HA in neutral solution at least partly through HA microcrystal disaggregation. The order of activity as measured by assay of calcium in the supernatant obtained from sedimentation at 46000xg was: hexametaphosphate (HMP) much greater than tripolyphosphate (TPP) much greater than ethane hydroxydiphosphonate (EHDP) approximately equal to methane diphosphonate (MDP) approximately equal to pyrophosphate (PP) greater than trimetaphosphate (TMP). Such activity might oppose the inhibition of acid demineralization of tooth enamel exerted by these compounds thus detracting from anti-caries activity. After binding to the HA surface, all of the polyphosphates underwent a slow hydrolysis, requiring several days at 37 degrees C for completion as measured by liberation of phosphate into water incubation medium. Hydrolysis in water solution was negligible under otherwise similar conditions; however, low concentrations of calcium catalyzed the hydrolysis in water solution suggesting that calcium in the HA crystal lattice or the hydration layer was responsible in the case of HA-bound polyphosphates. HA-bound phosphonates did not hydrolyze which would be anticipated since in these compounds the phosphate is combined through a carbon-phosphorus bond. We are presently attempting to determine rates of hydrolysis per mole of bound polyphosphate. Such hydrolysis could affect anticaries activity in two ways: (1) it would furnish a constant supply of phosphate to dental plaque which could inhibit demineralization or (2) it would gradually deplete the tooth surface of polyphosphate which would diminish caries protective activity. Since slow losses could be easily compensated for by reapplication of polyphosphate to the teeth, the advantages gained from phosphate liberation may predominate.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

1.0073, FACTORS AFFECTING TOOTH SURFACE MINERAL IN RELATION TO DENTAL CARIES

E. Stowell, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *5901 E. 7th St., Long Beach, California* 90822 (600-005-P)

Results of our studies with polyphosphates and phosphomates were reported in detail in the project report, entitled 'Effects of potential therapeutic agents on the formation and activity of dental plaque,' showing that, despite their anticaries effectiveness, these compounds caused some of the hydroxyapatite to dissolve and that polyphosphate binding to hydroxyapatite was followed by a gradual hydrolysis of the polyphosphate. A major effort is now being directed at the study of the effects of immiscible aqueous polysaccharide phases on adsorption to hydroxapatite. Having found that the adsorption of erythrocytes is influenced to a much greater degree by the polysaccharide interface than is the adsorption of hemoglobin, we are turning our attention to the effects on dental pellicle and plaque, starting with the adsorption of salivary proteins and bacteria to hydroxapatite powder. The influence of specific salt ions ionic strength, pH and phase ratios will be studied in an effort to arrive at an optimum phase system which may prove effective in decreasing, preventing or reversing the deposition of plaque on the tooth surface. Our aim is to complete this study within fifteen months, leaving open the possiblilty of expanding the project if the results show unusual promise.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

1.0074, INVESTIGATION OF CARIOUS LESIONS

A.S. Hallsworth, University of Leeds, School of Dentistry, Dept. of Oral Biology, *Blundell St., Leeds LS1 3EU, England, United Kingdom*

Interest in the Department in the changes occurring in the enamel of teeth after eruption both with respect to non-pathological changes and carious attack. A large number of investigations have been undertaken into the chemistry of sound enamel, the chemical changes associated with aging, and into the alterations brought about by carious attack.

Current interest centers on the characteristics of the developing lesion. New techniques of space replication together with recently developed microprocedures are facilitating these studies. Coupled with a general interest in the effect of fluoride on the tooth during development and afterwards, it is hoped that this work will lead to a greater understanding of the development of the carious lesion and the effect of fluoride and other agents upon the progress of carious attack.

SUPPORTED BY

University of Leeds	funds n.a.

ETIOLOGY - PLAQUE

1.0075, DENTAL PLAQUE OF FRUCTOSE-INTOLERANT PATIENTS

E. Newbrun, University of California, San Francisco Campus, School of Dentistry, Dept. of Oral Biology, *551 Parnassus Ave., San Francisco, California* 94122 (N01DE62498 (CONTRACT))

Study of a population of patients with a confirmed diagnosis of fructose intolerance from the standpoint of dietary intake, oral hygeine, and dental pathology. The microbiology of dental plaque from specific dental sites of these subjects will be investigated & particular attention will be given to dental plaque levels of S. mutans, S. sanguis and Lactobacilli. In addition, the concentration of protein, hexose, ketohexose, calcium, phosphorus, magnesium and fluoride in these plaque specimens will be assayed. The glucose metabolism of the plaque specimens will be investigated from the standpoint of levels and types of organic acids produced and levels of selected enzymes present.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0076, DENTAL PLAQUE AND SALIVA FROM GASTRIC INTUBATED PATIENTS

S.A. Ellison, Columbia University, School of Dental & Oral Surgery, Dept. of Oral Biology, *Broadway & W. 116th St., New York, New York* 10027 (N01DE92422 (CONTRACT))

Investigate a minimum of 25 gastric-intubated patients to perform detailed analysis of the microbiological, immunological, and biochemical constituents in dental plaque and saliva. Control subjects will be an equivalent number of age-matched volunteers who are staff, students, or patients at the Columbia-Presbyterian Medical Center. Samples will be taken from plaque which will be allowed to develop for four days after prophylaxis. Saliva samples will be collected after the initial cleaning prior to plaque accumulation.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$129,140

1.0077, ACQUISITION, TRANSMISSION AND LOCALIZATION OF HUMAN ORAL BACTERIA

R.J. Gibbons, Forsyth Dental Center, Dept. of Oral Microbiology, *140 Fenway St., Boston, Massachusetts* 02115 (P01 DE 02847-110020)

For summary: see 2.0048.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$59,216

1.0078, BIOCHEMICAL BASIS FOR THE CARIOGENIC PROPERTY OF STREPTOCOCCUS MUTANS

T. Shiota, University of Alabama in Birmingham, School of Dentistry, Dept. of Microbiology/Nutritional Sciences/Biochemistry, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130025)

OBJECTIVES: Mutants of S. mutans defective in their cell surface components or in their metabolic activities leading to altered cariogenicity in rats are being used to study the caries process. Research is being conducted to elucidate the role of specific cell surface sites involved in cell adhesion and cell aggregation in the plaque forming process. Research is also being performed to study the function of glucosyltransferase in cell adhesion and cell aggregation.

A mutant, C307, isolated from S. mutans strain 6715, was found to have lost its serospecific g antigen. This mutant, which was found to bind more glucan and glucosyltransferase than its parent type, was recently shown to be more cariogenic. This increase in cariogenicity was found in the main carious lesions associated with the lingual surfaces.

The results obtained with mutant C307 suggest that the sero-specific antigens are not involved in the attachment of S. mutans to surface of teeth.

In the future, additional mutants defective in cell surface structure will be sought and studied in order to learn about the formation of plaque and caries.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$82,429

1.0079, ANALYSIS OF NORMAL AND DISEASE-ASSOCIATED PLAQUE

W.J. Loesche, University of Michigan, Ann Arbor Campus, School of Dentistry, Dept. of Oral Biology, *Ann Arbor, Michigan* 48104 (R01 DE 03423-06)

Different types of dental plaque predispose to either caries or periodontal disease. Bacteria are intimately involved in both processes. Their role may be simply overgrowth in areas where hygiene cannot be maintained or certain bacteria may be etiologically responsible. The present proposal will examine both hypotheses as plaque will be removed from non-disease associated sites, and from caries associated sites. Pooling of plaque samples will be avoided so that the bacteriological and biochemical information obtained can be correlated with the clinical appearance of the sampled site. The plaques will be 1) examined bacteriologically either by screening for certain bacteria or by partially characterizing the predominant culturable isolates; 2) compared in their physiologic response to certain radioactive nutrients such as sucrose and glucose; 3) genotypes of S. mutans will be compared for carbohydrate metabolisms under varying conditions of pH, osmotic pressure and fluoride concentration.

BIBLIOGRAPHIC REFERENCES: Minah, G. E. and Loesche, W. J. Sucrose metabolism by prominent members of the flora isolated from cariogenic and noncariogenic dental plaques. Infect. and Immuniology 17, 55-61, 1977. Minah, G. E. and Loesche, W. J. Sucrose metabolism in resting cell suspensions of caries associated and noncaries associated dental plaques. Infect. and Immuniology 17, 43-54, 1977.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0080, ACTINOMYCES - MODEL STUDIES ON DENTAL PLAQUE FORMATION

O. Gabriel, Georgetown University, School of Medicine, Dept. of Biochemistry, *3800 Reservoir Rd. N.W., Washington, District of Columbia* 20007 (R01 DE 04201-03)

Studies on the cariogenic and non-cariogenic strains of Actinomyces viscosus are undertaken to provide basic information concerning peripheral structural elements of the bacterial cell wall. These peripheral structural elements are responsible for various cell surface related properties such as cell adhesion and immunological response. The first part of the study will be concerned with an extensive examination of catabolic enzymes capable of degrading the cell wall. Special emphasis will be placed upon the enzymatic degradation of peripheral cell wall components. Similarly, the catabolic degradation of extracellular polysaccharides of Actinomyces viscosus will be studied. In a complementary study to the above approach, we will concern ourselves with the biosynthesis of immunodeterminant sugars in Actinomyces viscosus and the incorporation of these sugars into the cell wall. Various attempts will be made to interfere with synthesis and/or incorporation of sugars into the cell wall.

It is the objective of our studies to provide a rational biochemical basis to correlate changes in peripheral structural elements of the cell wall with altered biological response. Bacterial cells with altered cell wall structures will be tested for their immunoresponse as well as their ability to adhere to the tooth.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0081, CALCULUS FORMATION USING CALCIFIABLE LIPOPROTEIN ANALOGUE

J.J. Vogel, University of Texas, Health Science Center at Houston, Dental Branch, *6515 Freeman, Houston, Texas* 77025 (R01 DE 04439-02)

Synthetic protein-acidic phospholipid complexes are being used to (1) define the mechanism of calculus calcification and (2) develop an assay for screening potential anticalculus agents. Kinetic studies using a lysozyme-phosphoinositide complex have shown that there is a rapid initial binding of calcium equivalent to 10 microgm/mg of complex which remains constant during the first 24 hours of incubation in a metastable calcium phosphate solution at 37C. The initial calcium binding is followed by a slower uptake of both Ca and HPO4 probably as an intermediate amorphous calcium phosphate phase and finally hydroxyapatite formation after 72 hours of incubation.

Once reliable kinetic data are obtained, the mode of action of various inhibitors will be evaluated. The procedure will allow us to determine whether inhibitors block initial calcium binding, interfere with formation of the amorphous intermediate phase or inhibits hydroxyapatite formation. Preliminary studies have shown that chlorotetracycline and diphosphoglyceric acid are effective inhibitors.

Similar data are also being obtained for calcifiable proteolipids isolated from microorganisms and vertebrate tissues. These correlative studies could provide valuable information for elucidating the mechanism of biologic calcification.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$28,657

1.0082, BACTERIAL COAGGREGATION MECHANISMS IN DENTAL PLAQUE

F.C. McIntire, University of Colorado, Medical Center, School of Dentistry, Dept. of Oral Biology, *4200 E. 9th Ave., Denver, Colorado* 80220 (R01 DE 04926-02)

The complex bacterial masses which develop on and adhere firmly to teeth, collectively known as dental plaque, provide most of the causes of dental caries and periodontal diseases. In the adherence of plaque, bacterial polysaccharides are important but we are only beginning to understand the variety of molecules, their nature and their interactions which are responsible for this phenomenon. A thorough understanding of these molecular interactions should lead to innovations for the removal of plaque or the suppression of its development, and thereby should contribute importantly to the control of dental caries and periodontal diseases.

Among the important interactions are numerous examples of specific coaggregation between bacteria of different species in plaque, e.g., Streptococcus sanguis and Actinomyces viscosus. S. sanguis is a very common, and often the most abundant bacterium identified in the early colonization of freshly cleaned teeth in man. Actinomyces, which are implicated in root caries and periodontal diseases, increase in number rapidly during the first several days of plaque formation. The coaggregation between these two may be important in the buildup of the Actinomyces population. The objective of this proposal is to provide an understanding of the molecular basis of coaggregation between S. sanguis 34 and A. viscosus T-14. We plan to: (1) Determine the conditions under which the coaggregation is reproducible, e.g., pH, specific ionic requirements, bacterial culture conditions, etc.; (2) Determine the nature of the molecules necessary for coaggregation; (3) Isolate the coaggregation molecules in highly pure form and determine the structural features of the specific reactive sites.

BIBLIOGRAPHIC REFERENCES: McIntire, Floyd C., Albert E. Vatter, Judy Baros and Julia Arnold. Studies on the Mechanism of Coaggregation between Actinomyces viscosus T14V and Streptococcus sanguis 34. In press, Infection and Immunity, IAI 163, for September 1978. Cisar, John O., Albert E. Vatter, and Floyd C. McIntire. Identification of the Virulence-Associated Antigen on the Surface Fibrils of Actinomyces viscosus T14. Infect. and Immun. 19:312-319, 1978.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $60,521

1.0083, DEVELOPMENT OF FISSURAL DENTAL PLAQUE

G.E. Minah, University of Maryland, Baltimore Professional Schools, School of Dentistry, Dept. of Microbiology, *66 W. Baltimore St., Baltimore, Maryland* 21201 (R23 DE 04795-03)

The objectives of this investigation are 1) to develop a removable dental model (RDM) for investigations of developing fissural dental plaque and 2) to clearly identify patterns of bacterial succession and changes in formation of major byproducts of carbohydrate metabolism in fissural dental plaque during normal dietary intake, during periods of high and low salivary exposure, during periods of exposure to high levels of sucrose or glucose, and during experimental induction of dental caries.

Dental student volunteers will fabricate and wear acrylic, Hawley-type, palatal appliances containing 2 to 4 occlusal segments of extracted teeth (the RDM) for periods of from 1 to 21 days. Salivary exposure of the fissures will be controlled by mechanical barriers in the fissures and substrate levels by application of minute quantities of sucrose or glucose to the chamber with 14C-labeled sucrose or glucose for 15 minutes. The major metabolic byproducts will then be quantitated. The bacteria will be dislodged from the inserts, cultured and identified. Caries formation in the central inserts will be determined by histological techniques.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $31,829

1.0084, BIOCHEMICAL PRODUCTS AND ENERGY REQUIREMENTS OF PLAQUE

S.A. Robrish, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00154-05 CPR)

We have completed the analysis of three adenine nucleotides, calculated the function of adenylate energy charge (AEC), and found it directly related to the percent viable cells in a pure culture of bacteria. Use of AEC analysis of viable cell mass is being assessed in dental plaque samples obtained from monkeys which have been treated with antiplaque agents. Protein content of plaque, conventional viable counting on bacteriological media, fluorescent antibody analysis for streptococci and actinomyces, and adenine nucleotide and AEC values are being compared. A computer program has been written to do the calculations for the nucleotide analyses.

BIBLIOGRAPHIC REFERENCES: Robrish, S.A., Kemp, C.W., Chopp, D.E., and Bowen, W.H. Viable and total cell masses in dental plaque as measured by bioluminescence methods. Clin. Chem., 1979. In press.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $64,342

1.0085, ASSOCIATION OF STREPTOCOCCUS MUTANS WITH DENTAL CARIES REDUCTION IN A SCHOOL POPULATION

L.A. Thomson, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00228-03 CPR)

Dental plaque is being studied to determine if changes in microorganisms, specifically strep. mutans, occur during fluoride preventive procedures. The school population consists of children using fluoride rinses either daily or weekly, as well as some children using placebo solution. Dental plaque samples are obtained periodically and analyzed using cultural methods and fluorescent antibody reagents specific for bacteria under study. Alterations in plaque composition during the study period will be related to the changes in the caries incidence.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$37,436

1.0086, THE STRUCTURE, GROWTH, METABOLISM AND BACTERIOLOGY OF PLAQUE ESPECIALLY IN RELATION TO DENTAL CARIES

Unknown, Medical Research Council, Dental Unit, *Bristol, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$165,353

1.0087, HUMAN DENTAL PLAQUE ORGANIC ACID PRODUCTION AND PH CHANGES, RELATED TO CARIES AND GINGIVITIS

D.A. Geddes, University of Glasgow, Dept. of Oral Medicine, *Glasgow G12 8QQ, Scotland, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$8,599

1.0088, ORIGIN AND ROLE OF ANIONIC MACROMOLECULES IN THE STRUCTURE AND FUNCTION OF DENTAL PLAQUE AND CALCULUS

G. Embery, University of Liverpool, Dept. of Dental Sciences, *P.O. Box 147, Liverpool L69 3BX, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$10,664

1.0089, DETERMINATION OF CA AND P ON PLAQUE

J. Reddy, University of Stellenbosch, Research Group in Dental Epidemiology, Dept. of Oral Pathology, *Private Bag 11, c/o Prof. C.W. VanWyk, Tygerberg 7505, Cape Province, South Africa*

The determination of Ca and P in special closely knit communities. An analyses of 36 hour plaque collected from the communities. The analyses have commenced in one community.

SUPPORTED BY

South African Medical Research Council	$3,000

1.0090, DETERMINATION OF FLUORIDE IN PLAQUE

A. Ferguson, University of Stellenbosch, Research Group in Dental Epidemiology, Dept. of Oral Pathology, *Private Bag 11, c/o Prof. C.W. VanWyk, Tygerberg 7505, Cape Province, South Africa*

The determination of fluoride in plaque from persons following a known diet and living under known conditions is undertaken. 36 hour plaque is collected and fluoride determined by electrode.

The research has commenced.

SUPPORTED BY

South African Medical Research Council	$1,500

ETIOLOGY - EXTRACELLULAR POLYSACCHARIDES

1.0091, PREPARE CULTURES OF EMBRYONIC CHICK LIMB CHONDROCYTES

A.I. Caplan, Case Western Reserve University, Case Inst. of Technology, Dept. of Biology, *2040 Adelbert Rd., Cleveland, Ohio* 44106 (N01DE72403 (CONTRACT))

For summary: see 2.0066.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$4,229

1.0092, CROSS-REACTING ANTIGENS/ORAL FLORA ACIDOGENIC BACTERIA

M.W. Stinson, State University of New York, Health Science Center at Buffalo, School of Medicine, Dept. of Microbiology, *3435 Main St., Buffalo, New York* 14214 (N01DE72408 (CONTRACT))

A study to search for antigens from nonpathogenic bacteria which cross-react with human oral strains of acidogenic streptococci, lactobacilli, and Actinomyces. Such antigens, if found, might afford more suitable alternative components of anticaries vaccines than cariogenic and acidogenic bacteria and their products.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$98,231

1.0093, INHIBITION OF DEXTRANSUCRASES OF CARIOGENIC ORGANISMS

E.E. Smith, University of Miami, School of Medicine, Dept. of Biochemistry, *1400 N.W. 10th Ave., Box 520875, Coral Gables, Florida* 33152 (R01 DE 03118-09)

The specific action of inhibitors on the extracellular dextransucrases elaborated by cariogenic Streptococcus mutans is being investigated in this project. Dextransucrases are secreted into culture media as a complex of several different enzymes and an important objective in this study is to devise a procedure to isolate in good yield and to purify to electrophoretic homogeneity, each of the specific components of the enzyme complex. The purified components will then be tested for their susceptibility to inhibition by various oxidized polysaccharides and oligosaccharides, which previously have been shown to be effective and specific inhibitors of the crude enzyme complex.

Results obtained from the purified enzymes should provide a better understanding of the mechanism of action of these inhibitors and hence, establish a rationale by which experiments may be devised for testing the potential therapeutic value of the action of individuals inhibitors on the formation of dental plaque by cariogenic organisms.

BIBLIOGRAPHIC REFERENCES: The Dextran Acceptor Reaction of Dextransucrase from Streptococcus mutans K1-R. Mead M. McCabe and Eric E. Smith. Carbohydrate Research, 63 (1978) 223-239.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$59,982

1.0094, STUDIES ON THE DEXTRAN SUCRASE OF STREPTOCOCCUS SANGUIS

R.M. Mayer, Ohio State University, Columbus Campus, School of Mathematics & Physical Sciences, Dept. of Chemistry, *164 W. 17th Ave., Columbus, Ohio* 43210 (R01 DE 03731-04A1)

The implication of Streptococcus sanguis in the process of caries formation, and the apparent intimate involvement of the microbial dextran in this process indicates that a thorough investigation of the enzyme responsible for its synthesis should be carried out. Dextran sucrase, an extracellular enzyme which catalyzes the transfer of glucose from sucrose to the growing dextran, is to be investigated, with regard to its mechanism, and the pathway of the reaction it catalyzes. The purpose of these studies is to provide an understanding of the reaction so that a rational approach to controlling the reaction can be made.

Two enzymes have been isolated from culture fluids, and in one case has been purified to homogeneity. This enzyme preparation will be used to continue studies on the mechanism of catalysis, on the mode of polymerization, and on the structural characteristics of the enzyme.

The formation of a glucosylated enzyme has been shown, and the proposed work will attempt to demonstrate that it is an obligatory intermediate. The nature of the linkage to the protein and the characteristics of the sugars present are to be studied. In addition knowledge of the amino acids at the active site will be sought. Questions concerning the direction in which polymerization occurs will be examined, as well as the basis for multiple types of bonding in the dextrans formed by the purified enzymes, by the utilization of substrate analogs.

The subunit structure of the enzyme will be examined under a variety of conditions.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$38,622

1.0095, CELL ADHERENCE OF DENTAL PLAQUE FORMING STREPTOCOCCI

M.M. McCabe, University of Miami, School of Medicine, Dept. of Microbiology, *1400 N.W. 10th Ave., Box 520875, Coral Gables, Florida* 33152 (R01 DE 04321-05)

The adherence of oral streptococci to oral soft tissues and to the tooth surface appears to involve highly specific mechanisms for host recognition and bacterial cell adherence. Studies in this laboratory suggest that carbohydrate-binding proteins (lectins) on the streptococcal cell surface specifically bind to oligosaccharides present in glycoproteins and glycolipids on the surface of host cells in the salivary glycoproteins of the dental pellicle. Adherence of Streptococcus mutans involves a somewhat modified version of this adherence mechanism since this organism synthesizes an adherent polysaccharide, dextran, from sucrose of the host diet and specifically binds to this polysaccharide, resulting in attachment of bacterial cells to the host tooth surface. Several dextran-binding proteins have been isolated from S. mutans. These include a lectin, two forms of dextransucrase and three minor proteins not yet identified. Continuing research is directed to the characterization of these streptococcal proteins and analyses of their roles in adherence of S. mutans. Additional studies will be directed to the identification, purification and characterization of lectins from several other oral streptococcal species and identification of the host carbohydrates involved in adherence of these organisms to host oral tissues and the dental pellicle. Proteins binding salivary mucin (bovine) have been isolated from a strain of Streptococcus sanguis and currently are being characterized.

BIBLIOGRAPHIC REFERENCES: McCabe, M.M., R.M. Hamelik and E.E. Smith. 1977. Purification of dextran-binding protein from Cariogenic Streptococcus mutans. Biochem. Biophys. Res. Comm. 78: 273-278. McCabe, M.M. and R.M. Hamelik. 1978. Multiple forms of dextran-binding proteins from Streptococcus mutans. Adv. Exp. Med. Biol. 107: 749-759.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$100,131

1.0096, MUTANT ANALYSIS OF THE ADHESION OF ORAL BACTERIA

J.D. Hillman, Forsyth Dental Center, Dept. of Microbiology, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 04529-03)

L(plus)-Lactate dehydrogenase-deficient mutants of Streptococcus mutans are being tested for their potential to serve as effector strains in the replacement theory of dental caries. Various studies have been performed, or are planned, to characterize both the pathogenic potential of the mutants and their ability to compete with naturally occurring strains of Strep. mutans in the oral cavities of susceptible hosts. In particular, it has been shown that the mutants produce less acid than their parent, BHT-2, from metabolism of glucose, sucrose, and a variety of other carbon sources, and hence should be less cariogenic. The mutants colonize the oral cavities of germfree and conventional Sprague-Dawley rats to the same extent as their parent, but produce a significantly lower incidence and severity of dental caries. Moreover, rats which have been colonized by a mutant strain appear resistant to superinfection by the parent strain. The ability of the mutants to exclude Strep. mutans of other serogroups is currently being studied. Similar studies of the pathogenic and competitive nature of the mutants are also being planned using monkeys as the host. Finally, the biochemical basis of the mutants' low acid-producing phenotype has been partially characterized, and it is hoped that a fermentation balance can be established for the metabolism of glucose.

BIBLIOGRAPHIC REFERENCES: Hillman, J.D. 1978. Non-reverting lactate dehydrogenase mutants of Streptococcus mutans. J. Dent. Res. 57A:270. Johnson, C.P., S. Gross, and J.D. Hillman. 1978. Cariogenic properties of LDH-deficient mutants of Streptococcus mutans. J. Dent. Res. 57A:270.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0097, ADHERENCE OF ORAL STREPTOCOCCI TO HYDROXYAPATITE

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Our overall objective is to define the mechanisms human dental plaque bacteria (specifically Streptococcus sanguis, Streptococcus miteor, Actinomyces viscosus and Actinomyces naeslundii) utilize to colonize the tooth surface. This requires a two phased study. First by characterizing the structure and specificity of the components produced extra-cellularly and/or on the bacterial surface which enhance their ability to adhere to the salivery pellicle. And secondly, the characteristics and identification of components from saliva that form the salivary pellicle and specifically bind to the bacteria.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$47,941

1.0098, DENTAL PLAQUE GLUCANOHYDROLASES AND CARIES FORMATION

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The specific objectives of the proposed study are: 1. To determine the relative proportion of glucanohydrolase producing microorganisms in the plaque and saliva of a selected population of children (0.0DMF as of 1974) using a newly developed microbial culture technique for differentiating bacteria capable of degrading various extracellular glucans. The distribution of these microbes will be correlated with the following data associated with these children: a) the level of cariogenic streptococci and other relevant microorganisms in saliva and site-specific plaque samples, b) the development of carious lesions, and c) a number of epidemiologic variables known or suggested to influence dental caries (age, sex, fluoride exposure, oral hygiene, etc.). 2. To define the oral microorganisms responsible for glucanohydrolase activity. This will be accomplished by: a) systematic bacterial taxonomy, b) studying the physiology of enzyme production with emphasis on examining potential hydrolase inducers compatible with the human metabolism, and c) separating the hydrolytic enzymes involved and determining their substrate specificity. 3. To assess the potential of oral glucanohydrolase producing microorganisms as natural agents to bacterial interference for the colonization of S. mutans. This will be approached in vitro by determining: a) the inhibition of water insoluble polysaccharide formation, and b) the inhibition of adhesions to either glass or specially prepared hydroxyapatite surfaces. An in vivo approach is described using sequential infection of hamsters with glucanohydrolase producing microbes and known cariogenic strains of bacteria.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0099, STUDIES ON THE REGULATION OF CARBOHYDRATE METABOLISM IN ORAL MICROORGANISMS

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The mechanisms by which various pathways of carbohydrate metabolism are regulated in oral bacteria continue to be under investigation. Currently, special emphasis is placed on: 1) characterization of the enzyme glucosyltransferase (GTase) produced by Streptococcus salivarius and 2) resolving the means by which the synthesis and secretion of this extracellular enzyme are controlled. The crude enzyme complex has been resolved into two catalytically active components. One (GTase I), produces a water insoluble polymer from sucrose while the other (GTase S) catalyzes the synthesis of a water soluble polymer from sucrose. Mutants have been isolated that are missing the GTase I component. Production of the extracellular GTase complex by S. salivarius is completely inhibited by cerulenin. This antibiotic has no effect on DNA, RNA or protein synthesis, but does severely inhibit cellular incorporation of acetate. It appears that GTase secretion is somehow closely linked to the de novo synthesis of long chain fatty acids.

BIBLIOGRAPHIC REFERENCES: Crow, V. L., and Wittenberger, C. L. Separation and properties of NAD- and NADP-dependent glyceraldehyde-3-phosphate dehydrogenases from Streptococcus mutans. J. Biol. Chem. 254: 1134-1142, 1979. St. Martin, E. J., and Wittenberger, C. L. Characterization of a phosphoenolpyruvate-dependent sucrose phosphotransferase system in Streptococcus mutans. Infect. Immun. 24: 865-868, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$161,120

1.0100, PHYSIOLOGICAL AND GENETIC STUDIES ON PATHOGENIC ORAL MICROORGANISMS

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The possibility that an endogenous endodextranase contributes to the structural complexity of the adherent and insoluble glucan synthesized from sucrose by oral streptococci is currently under investigation. For this purpose, Streptococcus salivarius mutants that produce either more or less dextranase have been isolated. Whereas the high-dextranase mutant synthesized about the same amount of insoluble glucan and produced adherent deposits like the parent, the low-dextranase mutant produced more soluble glucan and did not form adherent deposits. Two dextranase-deficient mutants of S. mutants 6715-13 have been identified and these also synthesized more soluble glucan. In order to determine whether these phenomena are causally related, the amounts of the glucosyltransferase enzymes producing soluble and insoluble glucan will be assessed. The possible role of plasmids in the physiology of S. mutants is being investigated also. As a result of these studies, two new species of circular DNA have been isolated from strain LM-7. The larger one is a 30Mdal covalently closed molecule, and the smaller one is a 2Mdal circular species, which is not a supercoil and which appears to originate from the previously described 3.6Mdal pAM7 plasmid.

BIBLIOGRAPHIC REFERENCES: Donkersloot, J. A., Flatow, U., Gibson, E., and Chassy, B.M.: Characterization of glucosyltransferase-deficient, plasmid-containing mutants of Streptococcus mutans LM-7. Infect. Immun. 21: 320-327, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$140,264

1.0101, STRUCTURE AND BIOSYNTHESIS OF PROTEOGLYCANS

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For summary: see 2.0078.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$56,506

1.0102, ADHERENCE AND COHERENCE OF CARIOGENIC STREPTOCOCCI IN DENTAL PLAQUE

J.E. Ciardi, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00195-04 CPR)

The mechanisms by which oral streptococci interact with teeth, saliva, and with each other to form cariogenic dental plaque are under investigation. Human or rat saliva depresses the adsorption of S. mutans serotype b and c cells to hydroxyapatite. Both types of saliva cause aggregation of only serotype c cells and appear to favor the adsorption of type c cells to hydroxyapatite. A rapid quantitative method to screen substances with a cariogenic potential has been developed. It measures growth, adherence and acid production by S. mutans. Mutants of S. mutans with diminished virulence and decreased ability to synthesize water-insoluble glucans adhered poorly to glass surfaces in the presence of sucrose. They were rendered as adherent as the parent strain following their exposure to glucosyltransferases that synthesized water-insoluble glucans. Human dental plaque formed in the presence of sucrose contained more lipoteichoic acid than plaques formed in the presence of glucose or xylitol. The importance of lipoteichoic acid in cariogenic dental plaque is being explored.

BIBLIOGRAPHIC REFERENCES: Ciardi, J.E., Reilly, J.A., and Bowen, W.H. Inhibition of sodium fluoride of 3H-glycerol incorporation into lipoteichoic acid in Streptococcus mutans. Caries Res. In Press, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$32,084

ETIOLOGY - MICROORGANISMS

1.0103, ORAL ENVIRONMENT OF A GNOTOBIOTIC CHILD

J.E. Novak, Baylor College of Medicine, School of Medicine, Dept. of Pediatrics, *1200 Moursund Ave., Houston, Texas* 77025 (M01 RR 00188-150114)

This project is part of a broader program (RR 00188-15) whose summary states: The objective of this proposal is to provide a multicategorical, multidepartmental Children's Clinical Research Center at Texas Children's Hospital. This facility will afford investigators an opportunity to carry out clinical research projects of high caliber on the pediatric subject and will provide a center for the integration of research efforts of many disciplines.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, Div. of Research Resources	funds n.a.

1.0104, EXPERIMENTALLY INDUCED DENTAL CARIES IN RODENTS

M.A. Taubman, Forsyth Dental Center, *140 Fenway St., Boston, Massachusetts* 02115 (N01DE42438 (CONTRACT))

The primary objective of this proposed research is to determine if immunization of rats with certain enzymes, from cariogenic bacteria, presented in a fashion to give rise to salivary IgA antibody, will result in effects on experimentally induced dental caries. The approach is to prepare crude enzyme antigens (CEA) from streptococci which have been shown to be cariogenic and to inject these antigens into the oral tissues of rats. After salivary and serum antibody response challenge is instituted with viable cariogenic Str. mutans, the dental caries scores are determined and compared in immunized and control animals. Saliva and serum are examined for enzyme-inhibitory capacity of antibody and oral tissues are examined for tissue antibody response as determined by fluorescent antibody techniques. A total of three experiments have been completed in conventional and gnotobiotic rats. In each of these experiments animals immunized with CEA demonstrated lower dental caries scores and carious lesions than comparable sham-immunized animals.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0105, ANTIBODY TO STREPTOCOCCUS MUTANS IN XEROSTOMIA PATIENTS

L.R. Brown, University of Texas, Health Science Center at Houston, Dental Branch, Dept. of Pathology, *6515 Freeman, Houston, Texas* 77025 (N01DE72402 (CONTRACT))

This contract represents new work utilizing saliva and serum samples collected over five years during performance of contract N01-DE-12377 with the Univ. of Texas. The examinations of saliva and serum for specific antibody activity of any kind were not done under this contract. However, saliva and serum samples of 42 xerostomia patients are still available and will be used for proposed study to measure with radiation-induced xerostomia. The Government envisions a period of performance of one year.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0106, ACQUISITION, TRANSMISSION AND LOCALIZATION OF HUMAN ORAL BACTERIA

J. van Houte, Forsyth Dental Center, Dept. of Oral Microbiology, *140 Fenway St., Boston, Massachusetts* 02115 (P01 DE 02847-110021)

The objective of the project is to gain information with respect to the oral colonization of potentially-cariogenic or predominant plaque organisms and their relation to dental disease. The studies involve in vitro as well as in vivo approaches with rodents and humans. Topics of study are: 1) The role of sucrose in the colonization of S. mutans on the teeth, 2) factors influencing the colonization of Actinomyces viscosus on the teeth, 3) studies of the effect of host age on the colonization of S. mutans and Actinomyces viscosus and the underlying mechanisms involved, 4) the influence of tooth enamel 'maturation' on the cariogenicity of acidogenic plaque organisms in rodents, 5) the role of acidogenic plaque bacteria, e.g. S. mutans, Actinomyces sp., lactobacilli in dental caries initiation and the in vitro study of their acidogenic properties, 6) the relation between the oral S. mutans levels of parents and their children, and, 7) the effect of locally administered antibiotics on the plaque levels of S. mutans.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$103,627

1.0107, MECHANISMS OF PATHOGENICITY IN TWO GROUPS OF PERIODONTOPATHIC BACTERIA

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The mechanisms of pathogenicity in two groups of periodontopathic bacteria will be investigated. 1. The surface components of Actinomyces viscosus (including antigens, other macromolecules and surface appendages) in a virulent strain (T14V) and its spontaneously occurring avirulent mutant (T14AV) will be isolated and characterized. The possible roles of these components in the virulence of these strains will be checked in several biological monitoring systems (in vivo and in vitro adherence-colonization studies, lysosomal enzyme release from polymorphonuclear leucocytes). 2. The major surface antigens and cytotoxic properties of three Gram negative crevicular bacteria -Bacteroides melaninogenicus 0381, Capnocytophaga isolates and an Actinobacillus (Y4)) will also be studied. Preparative immunoelectrophoresis and affinity-like organism chromatography will be used for isolation of major antigens and biological monitoring procedures (endotoxin activity, osteoclast activation, PMN effects, adherence to oral epithelia) will be used to assess biological significance of the isolated fractions. The taxonomic status of Y4 will be studied with emphasis on molecular approaches (DNA-DNA hybridization, DNA base composition, protein profiles and analysis of metabolic end products). The leucotoxic factor produced by Y4 will also be isolated, purified and characterized by immunologic and chromatographic methods. The role of plasmids as control mechanisms in several of these bacterial strains will also be investigated.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $127,211

1.0108, GENETIC AND BIOCHEMICAL BASIS FOR S. MUTANS VIRULENCE

R. Curtiss, University of Alabama in Birmingham, School of Dentistry, Dept. of Microbiology, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130033)

This research program is concentrated in two major areas: 1. Biochemical and Genetic Basis of S. mutans Pathogenicity: The goal is to utilize recombinant DNA technology to explore the biochemical and genetic bases of pathogenicity of Streptococcus mutans. Thus, S. mutans DNA is being cloned into suitable Escherichia coli K-12 hosts with plasmid and phage vectors to facilitate isolation and characterization of S. mutans gene products thought to be important in pathogenicity. 2. Arrangements and Regulation of Collagen Genes: An understanding of the genetic and biochemical processes involved in collagen biosynthesis is major goal of this research. However, more generally applicable knowledge of DNA structure and sequence arrangement, messenger RNA processing and protein synthesis in eukaryotic cells will result from these studies. For this purpose in vitro synthesized chick procollagen complementary DNA and native chick DNA sequences are being cloned into suitable E. coli K-12 hosts utilizing recombinant DNA technology. These clones will provide the genetic material necessary for the proposed studies.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $128,062

1.0109, SUCROSE METABOLIZING ENZYMES OF STREPTOCOCCUS MUTANS

H.K. Kuramitsu, Northwestern University, Chicago Campus, School of Medicine, Dept. of Microbiology & Immunology, *303 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 03258-08)

The molecular basis for the cariogenic properties of Streptococcus mutans will be investigated. Glucosyltransferase fractions synthesizing soluble and insoluble glucans will be purified to homogeneity and utilized to investigate the mechanism of adherent glucan formation. The interaction of these enzymes with phospholipids will be examined in order to assess the role of such interactions in the secretion and cell surface binding of the enzymes. It will also be of interest to investigate the role of enzyme-lipoteichoic acid complex formation on cell binding. Spheroplasts of S. mutans will also be prepared in order to investigate the synthesis and secretion of glucosyltransferases. Membrane fractions isolated from broken spheroplasts will also be utilized to examine the passage of the enzymes through this boundary and also to assess the role of intracellular invertase in the transport of sucrose.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $54,512

1.0110, INHIBITION OF HUMAN CARIOGENIC STREPTOCOCCI

G.D. Shockman, Temple University, School of Medicine, Dept. of Microbiology & Immunology, *3322 Broad St., Philadelphia, Pennsylvania* 19122 (R01 DE 03487-08)

This project will investigate various aspects of the nutrition, growth, physiology, biochemistry and ultrastructure of cariogenic streptococci as they are grown in liquid culture and as intact plaque in vitro. We intend to pinpoint conditions optimal for the sensitization of cariogenic streptococci to attack by chemical and other injurious agents.

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SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $60,975

1.0111, STREPTOCOCCAL SURFACE ANTIGENS AND DENTAL CARIES

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Previous studies have established the requirement for glucan synthesis from sucrose by glucosyltransferase on the surface of S. mutans to achieve in vitro adherence. Future studies will concern the nature of the surface of the S. mutans cell in relation to the function of the type specific polysaccharide and glucan as binding sites for glucosyltransferase. Con A and other lectins will be employed in these studies.

Efforts will also be made to further purify and chemically characterize the bacteriocin receptor sites on the surface of S. pyogenes and other streptococci. A common chemical component is shared by both sensitive and resistant strains. The binding of the bacteriocin and other data suggest the presence of immunity proteins. These studies relate to establishment of S. mutans in the oral cavity.

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SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0112, AMINO ACIDS AND CELL WALL BIOSYNTHESIS

Y. Chang, University of Maryland, Baltimore Professional Schools, School of Dentistry, Dept. of Microbiology, *66 W. Baltimore St., Baltimore, Maryland* 21201 (R01 DE 04116-03)

The objectives of this research project are to study the cariostatic effects of amino acids on in vitro plaque formation and cell wall biosynthesis, and to characterize the cell wall structure involved in the bacterial adhesive interaction and the attachment of glucosyltransferase in the cariogenic oral Streptococcus mutans. The research work will employ more refined assay methods for studying in vitro plaque formation in order to correlate this effect with the induction of sugar nucleotide accumulation, and peptidoglycan secretion resulting from amino acid treatment. The accumulated sugar nucleotide and peptidoglycan will be characterized to provide information for the cell wall structure affected by this treatment. Amino acid incorporation into cell wall and their cross-linking in the cell wall will also be studied along with other cell wall structural changes induced by amino acid treatment. N-acetylhexosamines and phytohemagglutinins will be used as specific blocking agents for the characterization of the cell wall receptor structure involved in the binding of glucosyltransferase. Studies will also be conducted to differentiate the dextran and glucosyltransferase binding sites and to examine the distribution of this enzyme under various treatments. Isotope-labeling techniques and various other new methodologies are also to be applied to achieve the specific goals proposed in this research project. S. mutans strain C67-1 and its non-cariogenic mutant strain C67-25 are also to be used for critical study of the various aspects proposed above.

BIBLIOGRAPHIC REFERENCES: Chang, Y. F. Lysine Metabolism in the Rat Brain.: The Pipecolic Acid-Forming Pathway. J. Neurochem. 30:347-354 (1978). Chang, Y. F. Lysine Metabolism in the Rat Brain: Blood-Brain Barrier Transport, Formation of Pipecolic Acid and Human Hyperpipecolatemia. J. Neurochem. 30:355-360 (1978).

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Services, Public Health Service,
National Inst. of Health,
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Research $0

1.0113, PHYSIOLOGY OF DENTAL PLAQUE BACTERIA

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A major part of the proposed work is a detailed investigation of the effects of fluoride ions on peptidoglycan synthesis in bacteria, with particular attention to bacteria found in dental plaque. Fluoride has been found to be a bacteriolytic agent when present in growth media. The responses of plaque bacteria to fluoride are in many respects similar to their responses to penicillin. Bacteria with highly active autolytic systems undergo lysis following growth in the presence of penicillin or fluoride. Bacteria without such active autolytic systems do not undergo lysis but do form defective cell walls. The action of fluoride appears to involve synthesis of abnormal peptidoglycan that is unusually sensitive to autolytic enzymes. We want to determine the specific biochemical reactions in peptidoglycan synthesis that are affected by fluoride and the nature of the abnormal product of synthesis.

Other parts of the project include development and exploitation of pellet culture systems for growing plaque bacteria in crowded conditions, further studies of ion-exchange reactions of plaque bacteria and work with plaque bacteria rendered hypersensitive to host defense mechanisms following growth in fluorideocontaining media.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0114, VARIATIONS IN THE SURFACE STRUCTURE OF ORAL BACTERIA

K.W. Knox, Inst. of Dental Research, *2 Chalmers St., Sydney, N.S.W., Australia* (R01 DE 04174-05)

We are using the chemostat for studying the effect of changes in growth condition on the surface components and extracellular products, particularly lipoteichoic acid, of cariogenic bacteria; changes being followed by chemical, serological and microscopic procedures. The organisms chosen are representative strains of streptococci, lactobacilli and actinomycetes, with studies initially concentrating on those strains whose cell wall carbohydrates--polysaccharides or teichoic acids--have been sufficiently characterized. These surface components are of importance in a) the identification of a particular organism and b) defining the nature of the organism's interaction with the environment. Lipoteichoic acid is a recognized component of the membrane of most gram-positive bacteria but it may also occur extracellularly in significant amounts.

The bacterial cell surface is particularly sensitive to changes in growth conditions Thus, by obtaining a clearer understanding of the effect of environmental conditions on the growth of cariogenic bacteria, we can better understand their role in inducing caries.

BIBLIOGRAPHIC REFERENCES: Knox, K.W., L.K. Campbell, N.A. Jacques and A.J. Wicken 1979. Extraction of antigenic components from oral streptococci. Pathogenic Streptococci, Ed. M.T. Parker. Reedbooks Ltd., England. in press. Knox, K.W., L.K. Campbell, K.W. Broady and A.J. Wicken 1979. Serological studies on chemostat-grown cultures of Lactobacillus fermentum and Lactobacillus plantarum. Infect. Immunity. April. in press.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$53,661

1.0115, VARIATIONS IN THE SURFACE STRUCTURES OF ORAL BACTERIA

A.J. Wicken, University of New South Wales, *P.O. Box 1, Kensington, N.S.W. 2033, Australia* (R01 DE 04175-05)

We are using the chemostat for studying the effect of changes in growth condition on the surface components and extracellular products particularly lipoteichoic acid of cariogenic bacteria; changes being followed by chemical, serological and microscopic procedures. The organisms chosen are representative strains of streptococci, lactobacilli and actinomycetes, with studies initially concentrating on those strains whose cell wall carbohydrates - polysaccharides or teichoic acids - have been sufficiently characterized. Lipoteichoic acid is a recognized component of the membrane of most gram-positive bacteria but it may also occur extracellularly in significant amounts. These surface components are of importance in (a) identification of a particular organism and (b) in defining the nature of the organism's interaction with its environment.

The bacterial cell surface is particularly sensitive to changes in growth conditions. Thus, by obtaining a clearer understanding of the effect of environmental conditions on the growth of cariogenic bacteria, we can better understand their role in inducing caries.

BIBLIOGRAPHIC REFERENCES: Knox, K.W., L.K. Campbell, N.A. Jacques and A.J. Wicken. 1979. Extraction of antigenic components from oral streptococci. Pathogenic Streptococci, Ed. M.T. Parker. Reedbooks Ltd. England. in press. Knox, K.W., L.K. Campbell, K.W. Broady and A.J. Wicken. 1979. Serological studies on chemostat-grown cultures of Lactobacillus fermentum and Lactobacillus plantarum. Infect. Immunity April issue. in press.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$58,242

1.0116, STUDIES ON THE GENETICS OF ORAL MICROFLORA

F.L. Macrina, Virginia Commonwealth University, School of Basic Sciences & Graduate Studies, Dept. of Microbiology, *901 W. Franklin St., Richmond, Virginia* 23284 (R01 DE 04224-05)

The 17 Mdal pAMbeta1 plasmid is known to confer erythromycin resistance in the streptococci. It is closely related to an apparently large family of such plasmids which are widely disseminated in several streptococcal Lancefield groups. pAMbeta1 may be readily introduced into Streptococcus sanguis via genetic transformation by direct selection for erythromycin resistance. S. sanguis is an exopolysaccharide-producing organism closely related to the cariogenic Streptococcus mutans in its ability to form adherent deposits (plaque) on smooth tooth surfaces. We have isolated a derivative of the pAMbeta1 plasmid which is 7.3 Mdal in size. The apparent deletion event which resulted in the formation of the 7.3 Mdal plasmid (desingated pZA1) occurred spontaneously in S. sanguis. pZA1 is cut once with a specific restriction endonuclease which yields single stranded overlapping ends. This plasmid thus is being tested as a vector in a 'self-cloning' S. sanguis system uisng standard recombinant DNA methods. Derivatives of pZA1 are being constructed by in vitro shortening of the plasmid molecule in order to develop improved cloning vectors in this system. All potential cloning vectors are being thoroughly characterized with respect to size, copy number, restriction nuclease sites, and ability to be amplified. These plasmid vectors will be used to develop a clone bank of the S. sanguis chromosome in a S. sanguis host. In this fashion, we hope to be able to locate and enumerate the genes involved in exopolysaccharide synthesis. These studies will contribute greatly to our understanding of the biochemistry and genetics of oral colonization by exopolysaccharide producing streptococci.

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SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$46,923

1.0117, LIPOTEICHOIC ACIDS--METABOLISM AND ROLE IN DENTISTRY

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The objectives of this project are to investigate the structure, biosynthesis, and secretion of lipoteichoic acids and the role of lipoteichoic acids in plaque formation. Such aims can be achieved by studying the structure, mechanism of biosynthesis and secretion of lipoteichoic acids in Streptococcus sanguis and the role of lipoteichoic acid in the adherence of cells on the tooth surface. S. sanguis is known to be the major streptococcal inhabitant on human tooth surface. We have found recently that there are large quantities of lipoteichoic acids present in the cell membrane and cell wall of S. sanguis. Our pulse chase study suggested that phosphatidylglycerol is a precursor for the synthesis of lipoteichoic acids. Moreover, the lipoteichoic acids were actively secreted into culture medium. Due to the amphipathic nature and high phosphate content of lipoteichoic acids, they may play important roles in the adherence of bacterial cells on the tooth surface. In this project the following four specific objectives will be pursued: (1) The structure of lipoteichoic acids. Attention will be focused on the structure of lipid moiety and glucosidic linkages. (2) Mechanism of lipoteichoic acid biosynthesis. In vitro system will be utilized to elucidate the stepwise reactions involved in the synthesis of membrane lipoteichoic acid. (3) The effects of various conditions on the secretion of lipoteichoic acids. The effects of pH, aeration, growth rate, on the secretion of lipoteichoic acids will be investigated. (4) The role of lipoteichoic acids on the adherence of bacterial cells on tooth surface. S. sanguis is known to possess a strong adherence ability to the tooth surface. The effect of purified lipoteichoic acid, lipoteichoic acid binding factors and antilipoteichoic acid antibody on the adherence of S. sanguis to enamel powder and the tooth surface will be investigated.

BIBLIOGRAPHIC REFERENCES: Biosynthesis of Oligosaccharide-lipid in Streptococcus Sanguis. T.H. Chiu and C. Saralkar. J. Bacteriol. 133, 185-195 (1978).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0118, CARIOGENESIS OF PLAQUE BACTERIA IN TEST MODELS

D.B. Fitzgerald, University of Miami, School of Medicine, Dept. of Microbiology, *1400 N.W. 10th Ave., Box 520875, Coral Gables, Florida* 33152 (R01 DE 04265-05)

This project seeks to determine the potential cariogenicity of human dental plaque microorganisms other than Streptococcus mutans by using a sequential screening procedure in animal model systems. The primary screen will involve hamsters receiving high sucrose Diet 2000. Representative strains of organisms which do not colonize the hamster on Diet 2000 will be retested in hamsters receiving a different cariogenic diet with a lower sucrose level. The final screen will be performed using monoinfections in gnotobiotic rats. In this way it is expected that it will be possible to identify any plaque organism which may contribute to caries development in humans. In addition to identifying potentially cariogenic plaque organisms, studies will be performed to determine biochemical and other cell characteristics which are associated with cariogenicity. This will include study of factors which enhance or diminish virulence of these organisms and the study of the effects of inhibitors of specific microbial metabolic reactions in vitro and in vivo. Organisms which are not readily identifiable by colonial morphology on selective media will be 'labelled' by induction of streptomycin resistance to facilitate determinations of how well they are able to colonize the hamster dentition since this would be a key prerequisite for any cariogenic microorganism. The use of a final screen in gnotobiotic rats will permit distinctions to be made between organisms which have no inherent cariogenic potential and those which do but are unable to establish themselves in the mixed microbial environment indigenous to the hamster.

BIBLIOGRAPHIC REFERENCES: Tanzer, J.M., and Fitzgerald, R.J. 1978. Lack of caries inhibitory property of 2-deoxy-D-glucose in rats. J. Dent. Res. 57: 440. Fitzgerald, R.J., and Fitzgerald, D.B. 1979. Cariogenicity of human oral lactobacilli in animals. J. Dent. Res. 58: (Special Issue A): A425 (Abstr. 1337).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$124,688

1.0119, PLAQUE BACTERIA AS PREDICTORS OF HUMAN DENTAL CARIES

B.A. Burt, University of Michigan, Ann Arbor Campus, School of Public Health, Community Health Programs, *Ann Arbor, Michigan* 48104 (R01 DE 04504-01A2)

The study aims to delineate the extent to which colonization of S. mutans, S. sanguis, and organisms of the lactobacillus species precede the clinical manifestation of fissure caries. It will also examine the quantitative relationship between these organisms, over time, in both clinically sound and in clinically carious teeth. The time sequence of colonization of the organisms, both in absolute terms and relative to each other, will be related to the development, or absence of development, of clinical caries, and the study will seek to demonstrate microbiological developments that predict the diagnosis of clinical caries with a high degree of probability. In addition, the study will seek to validate a simple predictive test for dental caries, suitable for use in the dental office. This test is based on the ratio of S. mutans to to S. sanguis (MS ratio) in the plaque sample. This three year longitudinal study is an epidemiological-microbiological collaboration. Approximately 500 children in the nonfluoridated community of Coldwater, Michigan, are expected to begin the study. Each child will have individual plaque samples taken from the occlusal fissures of initially caries-free mandibular first molars at six-month intervals, and will receive a clinical dental examination each year. Part of each plaque sample will be plated out, incubated, and a count made of colony-forming units resembling S. mutans, S. sanguis, and lactobaccilli. For the predictive test, another part of the sample will be incubated in a mannitolarginine broth, which changes color above a certain MS ratio. Results of the bacterial counts will be compared with the carious status of the teeth as determined by the clinical examinations, and results from different examination and sampling cycles compared. Results of the color-change test can be validated against the bacterial counts.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$90,028

1.0120, STREPTOCOCCUS SANGUIS RECEPTORS FOR SALIVARY GLYCOPROTEIN

M.J. Levine, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (R01 DE 04518-04)

The purpose of this proposal is to continue our studies on the specificity of interaction of salivary glycoproteins with oral Streptococci. Glycoproteins which will be studied include mucin, lactoferrin, and secretory IgA. Streptococci to be studied include representative strains of the three seroytpes of Streptococcus sanguis as described in Rosan, 1974. Studies will be aimed at determining what portion of each salivary glycoprotein (ligand) is responsible for interactions with the representative strains of S. sanguis. The specific salivary ligand will then be utilized to isolate the bacterial surface receptor involved in this interaction. Isolation will be performed using affinity chromatography techniques. Purified surface receptors will then be characterized with respect to their chemical composition and physical properties.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $98,991

1.0121, LASER HOMODYNE STUDY OF PLAQUE BACTERIA AGGREGATION

R. Schiller, Stevens Inst. of Technology, Graduate School, Dept. of Physics & Engineering Physics, *Castle Point Station*, *Hoboken*, *New Jersey* 07030 (R01 DE 04559-02)

During this coming year we plan to continue our laser homodyne scattering study of the effects of saliva on bacterial aggregation. In the next 2 months we expect to have detailed experimental information on the aggregating characteristics of bacteria suspended in saliva from caries-resistant and caries-prone individuals, as well as differences in activity between the submaxillary and parotid fluids. If these experiments confirm our preliminary data, we may be able to develop a clinical testing procedure for identifying caries-prone children.

In the coming year we shall attempt to identify isolated specific factors such as glycoproteins which may be responsible for the observed changes. We also plan to analyze the significance of interactions between different plaque bacteria in establishing aggregate size, structure and stability.

We expect to study the effects on aggregation of oral factors such as secretory IgA, calcium, dextran, etc.

We wish to determine the adherence strength of bacteria to solid substrates and the aggregation characteristics of bacteria suspended in ground enamel or hydroxyapatite as a function of bacterial species and different environmental factors such as saliva, dextran, etc.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0122, TRACE METAL UPTAKE IN CARIOGENIC STREPTOCOCCUS MUTANS

B.R. Byers, University of Mississippi, Medical Center, School of Medicine, Dept. of Microbiology, *2500 N. State St.*, *Jackson*, *Mississippi* 39216 (R01 DE 04903-01A1)

The objectives of this research are: 1. To define the requirements for and effects of certain metal ions (trace metals), including calcium, manganese, magnesium, iron, copper, cobalt, zinc and tin on growth parameters of the cariogenic organism Streptococcus mutans. These experiments will be conducted in continuous cultures in chemostat using chemically defined medium (treated to lower trace metal contamination and supplemented with high purity trace metals) under controlled conditions of substrate concentration, trace metal additions, oxygen tension, and pH. 2. To determine the mechanisms of uptake and transport of the above metal ions through kinetic studies for definition of metal ion transport systems and to measure the affinities, specificities, and energy dependence of these systems.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $37,579

1.0123, CHARACTERIZATION OF SURFACE ANTIGENS OF S. MUTANS

R. Linzer, State University of New York, Health Science Center at Buffalo, School of Dentistry, *3435 Main St.*, *Buffalo*, *New York* 14214 (R01 DE 05017-01A1)

The objective of this research proposal is to increase our knowledge of the antigens that are present on the cell surface of Streptococcus mutans since this knowledge is an essential basis for immunoprophylactic studies related to dental caries. This will be done by characterizing the rhamnose-containing polymers (RCP) that are present in the cell walls of S. mutans serotypes a, d, and g strains.

The RCPs will be extracted from cell walls using hot acidic conditions, chromatographically purified, and chemically characterized. The immunogenicity of the RCPs will be examined using a passive hemagglutination assay to screen antisera to whole cells and RCP-wall preparations for antibodies that are specific for the RCP. Both reactivity among the RCPs and between the RCPs and the serotype-specific polysaccharides (SSP) of S. mutans. Agar gel diffusion, tandem cross-immunoelctrophoresis, and the passive hemagglutination assays will be used in these studies. The specificity of the antigenic determinants on the RCP will be examined by inhibition studies utilizing di- and tri-saccharides isolated and characterized from partial acid hydrolysis of the RCP. Immunoelectron microscopic studies will be used to verify the localization of the RCP and the SSP in the microcapsular or cell wall material of S. mutans. Semi-quantitative changes in these surface antigens in response to differences in growth media will also be observed.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $40,006

1.0124, CELL ENVELOPE SYNTHESIS AND CONTROL OF ORAL MICROBES

T. Chiu, University of Pittsburgh, School of Dental Medicine, Dept. of Microbiology, *C336 Salk Hall, Pittsburgh, Pennsylvania* 15213 (R01 DE 05018-02)

Cell wall, because of its ability to confer rigidity and shape, is one of the most important structural features of the procaryotic cells. Although the mechanism of biosynthesis of several complex saccharides has been well established in the past decade, the mechanism involved in the biosynthesis of cell wall polysaccharide and its incorporation into the peptidoglycan is not understood. The objective of this project is to investigate the stepwise biosynthesis of the peptidoglycan-polysaccharide complex in Streptococcus sanguis and other oral streptococci. It is hoped a common precursor could be identified and utilized for the control of these bacteria. Recently we have been able to incorporate the individual sugar components of cell wall polysaccharide into polyisoprenyl-phosphate lipid. Several unique features could be shared by the synthesis of wall teichoic acid as judged from the reports of other laboratories.

In this proposal the following specific aspects will be investigated: 1. Further characterization of the monosaccharide-lipid. 2. The mechanism of biosynthesis and characterization of the lipid intermediates involved in the wall polysaccharide synthesis of S. sanguis and other oral bacteria. 3. Incorporation of the polysaccharide chain into peptidoglycans. 4. Inhibition of the wall biosynthesis by interfering with the utilization of the common precursors.

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National Inst. of Health,
National Inst. of Dental
Research $25,565

1.0125, BINDING OF FLUORIDE BY CARIOGENIC BACTERIA

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Reports indicate that additions of fluoride to communal water supplies reduced significantly the incidence of dental caries. In a number of instances anticariogenicity has been shown to arise from retardation of fermentation of dietary carbohydrate by oral bacteria. The major problem in interpreting the effects of fluoride on bacterial metabolism is the lack of information related to the definition of the site of binding of fluoride, the type of microorganisms that bind fluoride, the quantity of fluoride bound by oral bacteria and the conditions under which fluoride binding occurs. It is to these fundamental problems mentioned above to which this investigation is being directed.

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Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $46,452

1.0126, CARIOGENIC MECHANISMS OF GINGIVAL PLAQUE BACTERIA

H.K. Kuramitsu, Northwestern University, Chicago Campus, School of Medicine, Dept. of Microbiology & Immunology, *303 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 05141-01)

The molecular basis for the proposed cariogenic properties of Actinomyces viscosus will be investigated in this proposal. The specific attachment of the organism to cemental surfaces and epithelial cells will be examined utilizing in vitro assay systems. The role of levans, extracellular slime or other macromolecules in the specific adherence mechanisms will be examined primarily by utilizing mutants of A. viscosus defective in synthesizing individual polysaccharide molecules. This approach will also be utilized to determine the role of these polysaccharides in the specific aggregation of A. viscosus to Veillonella alcalescens. The glucan binding protein of A. viscosus will be characterized following purification on glucan-affinity columns. Antibody directed against this component will be utilized to examine the significance of the protein in cariogenicity. The role of plasmids in glucan binding will be assessed by determining the presence or absence of these elements in spontaneous or induced non-glucan binding variants. Finally, the molecular basis of levan metabolism by A. viscosus will also be determined. The enzymes involved in levan metabolism will be characterized and the mode of regulation of these enzymes determined.

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Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $79,944

1.0127, ORAL BACTERIA, PROTEASES AND HUMAN SALIVARY PROTEINS

S. Choih, University of Minnesota, Minneapolis Campus, School of Dentistry, Dept. of Oral Biology, *6 Morrill Hall, Minneapolis, Minnesota* 55455 (R23 DE 05071-02)

Preliminary studies have demonstrated that enzyme activities from oral bacteria can degrade anionic proteins from human parotid and submandibular gland saliva. Several of the modified proteins are proline-rich. In addition, it was discovered that the enzyme PZ-peptidase is produced in large amounts by oral streptococci and actinomycetes. The specific objectives of this proposal are: 1. To determine by microbiological methods the bacteria in human saliva and plaque which are able to produce significant quantities of PZ-peptidase and other enzymes with the capacity to modify gland saliva proteins. 2. To purify by biochemical fractionation methods, such as affinity chromatography, the PZ-peptidase and other protease activities from specific oral bacteria. 3. To test the effect of purified PZ-peptidase and other proteases on the proline-rich proteins in parotid gland saliva. The substrate specificity of PZ-peptidase and the known sequence of amino acids in the proline-rich proteins makes it likely that such cleavage occurs. 4. To determine if proteases from oral bacteria are able to modify saliva proteins known to be involved in regulating the ecology of the oral flora and cell-associated proteins believed to be involved in heterotypic bacterial adherence.

BIBLIOGRAPHIC REFERENCES: Choih, S-J., Smith, Q. T., and Schachtele, C. F. (1978). Modification of human parotid saliva proteins by oral Streptococcus sanguis. J. Dent. Res., in press. Choih, S-J., and Schachtele, C. F. (1979). Survey of PZ-peptidase production by oral bacteria. Int. Assoc. Dent. Res. Abstr. 1979, in press.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $11,903

1.0128, UTILIZATION OF CARBOHYDRATES BY ORAL BACTERIA

B.M. Chassy, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Laboratory of Microbiology & Immunology, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00042-09 LMI B)

The metabolism of sucrose and lactose has been studied because of these sugars involvement in supporting the formation of dental caries in conjunction with the growth of Streptococcus mutants and Lactobacillus casei. Sucrose can be transported into S. mutants cells by the action of a PEP-PTS activity with the production of intracellular sucrose-6-phosphate (S6P). S6P has been chemically synthesized, and an enzyme catalyzing it is apparently identical with the previously described intracellular invertase. A fructokinase that catalyzes the ATP-dependent phosphorylation of fructose has been characterized as well. In L. casei it has been shown that lactose is transported into the cell by a specific lactose PEP-PTs; the resulting lactose-6-phosphate is cleaved by phospho-beta-galactosidase to glucose and galactose-6-phosphate. It has been shown that these first two steps of the metabolism of lactose are plasmid-coded. Several distinct lactose plasmids have been identified and their genetic potential and inter-relatedness is under investigation.

BIBLIOGRAPHIC REFERENCES: Chassey, B. M., E. M. Gibson and A. Giuffrida (1978), evidence for Plasmid-Associated Lactose Metaabolism in Lactobacillus casei subsp. casei, Current Microbiology I, 141-144. Chassey, B. M. and E. V. Porter (1979). Initial Characterization of Sucrose-6-Phosphate Hydrolase and its Apparent Identity with Intracellular Invertase. Biochem. Biophys. Res. 89: 307-314.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $154,502

1.0129, LECTINS IN THE STUDY OF PLAQUE AND CARIES DEVELOPMENT

D.B. Mirth, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Preventive Methods Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00147-05 CPR)

Lectins, which are proteins capable of interacting with certain macromolecules and/or cell types via specific sugar moieties, are being used to investigate the interactions between saliva and/or bacteria in order to better elucidate the role these interactions play in plaque and caries development. Findings to date support the conclusion that 4 lectins, wheat germ agglutinin, concanavalin A, fucose binding protein and soybean agglutinin, can reversibly bind to and inactivate by complexation and/or precipitation the aggregating factor in saliva that is responsible for inducing the aggregation of Streptococcus mutans cells. These results provide evidence that the salivary aggregating factor contains N-acetyl-D-glucosamine, D-mannose and/or D-glucose, L-fucose and N-acetyl-D-galactosamine and/or D-galactose. Chromatographic and immunochemical techniques are being investigated for the isolation and characterization of the salivary aggregating factor contained in the lectin-induced precipitates.

BIBLIOGRAPHIC REFERENCES: Mirth, D.B., Miller, C.J., Kingman, A., and Bowen, W.H. Inhibition of saliva-induced aggregation of Streptococcus mutans by wheat germ agglutinin. Caries Research. 13: 121-131, 1979. Mirth, D.B., Miller, C.J., Kingman, A., and Bowen, W.H.: Investigation of salivary aggregating factors with lectins. In Kleinberg, I., Ellison, S.A., and Mandel, I.D. (Eds.): Saliva and Dental Caries. Sp. Supp. Microbiology Abstracts, pp. 255-266, 1979.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$61,414

1.0130, THE ROLE OF PLASMIDS IN THE PATHOGENESIS, ECOLOGY AND TAXONOMY OF THE ORAL MICROFLORA

D.J. LeBlanc, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Microbiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00174-04 LMI)

A rapid, inexpensive and highly reproducible procedure for the detection and isolation of plasmid DNA from virtually any species of Streptococcus was developed and used to screen 124 tetracycline resistant streptococci, from the oral cavity of periodontal patients, for the presence of plasmid DNA. Plasmids were detected in only 21% of these isolates, suggesting that tetracycline resistance among the oral streptococci is, for the most part, not plasmid-mediated. Using the same procedure, together with standard plasmid curing techniques, data were obtained which suggested that among strains of the group N streptococcus, S. lactis, plasmids play a role in the metabolism of at least six different carbohydrates. The new isolation procedure was also used in the examination of the molecular properties of a deleted antibiotic resistance plasmid in a strain of S. anginosus. The transmissible R factor, pAM beta 1, was shown to have lost approximately 50% of its DNA. The resultant molecule was no longer transmissible by conjugation, but still mediated resistance to erythromycin and lincomycin. In addition, the deleted plasmid existed in two unusual molecular configurations.

BIBLIOGRAPHIC REFERENCES: LeBlanc, D. J., Crow, V. L., Lee, L. N. and Garon, C. F.: Influence of the lactose plasmid on the metabolism of galactose by Streptococcus lactis. J. Bacteriol. 137: 878, 1979. LeBlanc, D. J., Hawley, R. J., Lee, L. N. and St. Martin, E. J.: Antibiotic-resistance plasmids among the oral streptococci. In Parker, M. T. (ed.). Pathogenic Streptococci. Reedbooks, Surrey, England. p. 286, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$109,920

1.0131, A GENETIC ANALYSIS OF METABOLIC PATHWAYS IN VARIOUS MEMBERS OF THE ORAL MICROBIAL FLORA

E.J. St. Martin, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Microbiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00208-03 LMI)

Several metabolic pathways present in Streptococcus mutans have been examined using mutant analysis techniques. Two enzyme systems for ammonia assimilation have been identified: glutamate dehydrogenase and the coupled reactions of glutamine synthetase and glutamate synthase. The primary pathway for sucrose utilization has also been determined. Catabolism of sucrose is initiated by an inducible phosphoenolpyruvate-dependent sucrose phosphotransferase system followed by an intracellular sucrose 6-phosphate hydrolase.

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In M. T. Parker (ed). Pathogenic streptococci. Reedbooks Ltd., Surrey, England, 1979.

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National Inst. of Health,
National Inst. of Dental
Research $56,613

1.0132, CARIOGENICITY OF THE DIFFERENT SEROTYPES OF S. MUTANS IN GNOTOBIOTIC RATS

W.A. Little, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00263-01 CPR)

A series of experiments is underway with gnotobiotic rats to determine the relative cariogenicity of the different serotypes of S. mutans.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $5,162

1.0133, MICROBIAL COMPOSITION OF DENTAL PLAQUE FROM IRRADIATED PRIMATES

C. Emilson, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00270-01 CPR)

Plaque samples from four irradiated monkeys and from four controls were analysed by using fluorescent antibody (FA) reagents specific for S. mutans, S. sanguis, S. salivarius, lactobacilli, Actinomyces and B. melaninogenicus. The irradiated animals showed a higher proportion of S. mutans and a lower proportion of S. sanguis when compared with that in the controls.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $11,138

1.0134, CELL WALLS OF ORAL STREPTOCOCCI

A.S. Bleiweis, State University System of Florida, University of Florida, Agricultural Experiment Station, Dept. of Bacteriology, *Gainesville, Florida* 32601 (FLA-BC-01440)

OBJECTIVE: Determine biochemical and immunochemical structures of cell walls of several unidentified strains of streptococci indigenous to the mammalian oral microbiota and classify these unknown microbes.

APPROACH: Extract cell walls of Streptococcus mitis and carious strains HS-6, FA-1 and K1R by glass-bead breakage of cells; determine qualitative and quantitative chemical compositions of each cell wall type after acid hydrolysis. Extract antigenic macromolecules from cell walls by enzymatic means and purity of column chromatography; verify purity of antigenic polymers by physico-chemical analyses; characterize each antigen by quantitative chemical analysis and haptenic-inhibition of serologic reactions. Check for serologic cross-reactions and compare analyses for each strain in order to classify into serologic subgroups.

PROGRESS: Two polysaccharide antigens were extracted chemically from cell walls of Streptococcus mutans AHT (serotype a) and B13 (d). After purification by affinity chromatography on columns containing the galactose-specific castor bean lectin, each product was found to be a diheteroglycan of galactose and glucose. The a antigen is determined immunologically by D-galactose linked 1 yield 6 to the adjacent sugar while the d antigen is determined by D-glucose linked 1 yield 6 to its neighbor. The antigens were cross-reactive due to a common (a-d) hapten composed of D-galactose linked 1 yield 6 to a sub-terminal sugar. Methylation analysis revealed major structural similarities between the two macromolecules: each contains the a equal to d hapten as part of a short branch off an internal galactose, while the specifc (a,d) haptens are part of the linear portion of the polymers. Models of each have been proposed. Also, the lipoteichoic acid (LTA) of AHT was isolated and purified by a unique method. Phenol-water extracts of whole cells were grossly contaminated with the a polysaccharide. Classical chromatography failed to separate these polymers. Synthetic vesicles prepared using phosphatidyl choline were found to bind the LTA while polysaccharides were removed by washing. After dissolving the liposomes in methanol-chloroform, the purified LTA was recovered by aqueous precipitation. Over 80% of the measurable LTA was recovered by this simple technique.

SUPPORTED BY
Florida State Government funds n.a.

1.0135, THE INCIDENCE, FINE STRUCTURE, PROPERTIES AND ROLE IN ADHERENCE OF FIMBRIAE ON ORAL STREPTOCOCCI

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No summary has been provided to the Smithsonian Science Information Exchange.

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Medical Research Council $11,345

1.0136, NITROGENOUS METABOLITES OF MICROORGANISMS IN DENTAL PLAQUE

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No summary has been provided to the Smithsonian Science Information Exchange.

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Medical Research Council $12,025

ETIOLOGY - SALIVARY FACTORS

1.0137, EVALUATION OF FACTORS IN SALIVA AND PLAQUE OF CARIES-FREE RECRUITS OF POTENTIAL THERAPEUTIC APPLICABILITY FOR PREVENTATIVE DENTISTRY

B.L. Lamberts, U.S. Dept. of Defense, Navy, Naval Dental Research Inst., Biochemistry Div., *Great Lakes, Illinois* 60088 (DN977593)

Approximately 2 percent of naval recruits enter the service without ever having had dental decay. These men require one-third fewer dental treatment procedures than their fellow recruits, reducing substantially the man hours and resources necessary to prepare them to a state of combat readiness. This unique population of decay-free young adults provides a special opportunity to evaluate the factors responsible for their resistance to oral disease. This could lead to new measures that could be applied toward the preventative dental care of Navy and Marine Corps personnel.

The significance of oral bacterial glucanases as protective factors against decay-producing organisms will be evaluated. A basic salivary peptide, sialin, which affects bacterial metabolism has been identified and its relationship to dental caries susceptibility will be determined. The potential of basic salivary proteins to counteract deleterious byproducts of decay-producing organisms will also be evaluated for application to clinical preventive dentistry treatments.

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1.0138, SALIVARY IMMUNOGLOBULIN A DEFICIENCY & DENTAL CARIES

J.R. McGhee, University of Alabama in Birmingham, School of Dentistry, Institute of Dental Research, *1919 7th Ave. S., Birmingham, Alabama* 35233 (N01DE52456 (CONTRACT))

The Contractor proposes to study a population of more than 25 IgA deficient patients and appropriate controls to correlate the presence or absence of IgA and caries incidence. He will measure salivary immunoglobulins and factors such as lysozyme, lactoferrin, and peroxidase. Plaque will be collected and analyzed for the principal oral bacteria present. Plaque proteins will be studied from the standpoint of in situ function-possible coating and/or aggregation of important plaque bacteria. He will correlate these findings with the clinical picture occurring in these patients, including past and present caries, and gingival and Periodontal Disease indices.

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National Inst. of Health,
National Inst. of Dental
Research $189,515

1.0139, DENTAL DISEASES AND DIET - INFLUENCE OF NUTRITION ON THE DEVELOPMENT, HEALTH, AND FUNCTION OF ORAL AND PARA-ORAL STRUCTURES

B.S. Worthington, University of Washington, School of Dentistry, Dept. of Oral Biology, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P50 DE 02600-130004)

The nutrition project underwent a gradual phaseout during the past year and in the process no new research was instigated. Past research findings were prepared for publication and this is still underway; effort is being made to compare the responses observed in infant monkeys in the CROB-supported project with the responses observed by Dr. Olav Alvares in young adult monkeys in the NIDR-supported project related to protein-calorie malnutrition and oral response.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,

National Inst. of Dental Research	$704

1.0140, STUDIES ON HUMAN PAROTID PROTEINS

P.J. Keller, University of Washington, School of Dentistry, Dept. of Oral Biology, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P50 DE 02600-130009)

The program of research is the result of a long-standing interest in the secretion of protein. It consists of two major studies. I. A continuation of earlier studies of the proteins secreted by human salivary glands, with emphasis on a group of basic proline-rich proteins whose function is presently unknown. The physiological role of these proteins, and their chemical structure is under study. II. Studies aimed at gaining insight into the molecular mechanism of membrane fusion and resorption as observed during the secretory cycle in rat parotid glands.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$75,009

1.0141, MEMBRANE DYNAMICS IN THE SALIVARY EXOCRINE CELL

M.R. Robinovitch, University of Washington, School of Dentistry, Dept. of Oral Biology, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P50 DE 02600-130016)

The research proposed in this grant application is aimed at gaining information concerning the origin, fate, chemical and physical nature, and biochemical activity of the secretory granule membrane in the salivary exocrine cell, thereby to attain a further understanding of the regulatory mechanisms involved in the synthesis, storage and release of the material enclosed by this membrane.

The specific aims are: (1) to determine whether the secretory granule membranes are synthesized de novo with each new generation of secretory granules or whether they are derived from pre-existing membrane via recycling, (2) to determine if the secretory granule membrane and the other types of membranes in the acinar cells possess morphological or structural markers which may allow us to follow the origin and fate of the secretory granule membrane, and/or give us insight into the mechanisms of membrane fusion and resorption which appear to be essential events during the secretory cycle, (3) to characterize the secretory granule membranes and the other membranes of the acinar cells chemically and enzymatically in order to find specific markers which may allow us to follow the origin and fate of the secretory granule membrane and/or provide insight into the mechanisms of membrane fusion and resorption in these cells.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$34,904

1.0142, ION TRANSPORT IN SALIVARY GLANDS - PERMEABILITY OF ORAL MUCOSA

E.L. Watson, University of Washington, School of Dentistry, Dept. of Oral Biology, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P50 DE 02600-130019)

Studies on the relationship of calcium to secretion in submandibular glands: Our studies to date have been concerned with calcium uptake and release from a microsomal fraction prepared from this gland and how secretory stimulants affect these processes. These studies are now being expanded into experiments concerned with the effects of pharmacological agents on unidirectional calcium fluxes and amylase release using a tissue-slice system.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$46,355

1.0143, TOOTH-SALIVA INTERFACE PHENOMENA AND DENTAL CARIES

D.I. Hay, Forsyth Dental Center, Dept. of Chemistry, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 03915-06)

Recent research has established that a complex system exists in human saliva which plays an important role in the maintenance, protection and repair of the dental enamel. The key feature of this protective system is the presence, in the saliva, of supersaturated, but stabilized concentrations of calcium and phosphate ions. This stabilization is maintained by at least two unusual salivary macromolecules, which act by inhibiting precipitation of calcium phosphate salts from the supersaturated saliva. A further part of this system consists of a thin film of selectively absorbed salivary proteins, known as the acquired enamel pellicle, which is present on all enamel surfaces, and which prevents the deposition of calcium phosphate minerals from the supersaturated saliva onto the teeth.

This system provides important protection against dental caries, by suppressing enamel dissolution and mineral transport during carious attack, and by recalcifying at least some early carious lesions. Also, microbiological degradation of the inhibitory macromolecules appears to be a factor in calculus formation, and therefore important in periodontal disease. The purpose of the proposed research is to identify and characterize the salivary precipitation inhibitors, and to determine their mode of action. From this research will come an improved understanding of the relationships which exist between the dental enamel and the oral environment, in both health and disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$109,130

1.0144, EFFECT OF SALIVA ON THE METABOLISM OF DENTAL PLAQUE

I. Kleinberg, State University of New York, Health Science Center at Stony Brook, School of Dentistry, Dept. of Oral Biology & Pathology, *Stony Brook, New York* 11790 (R01 DE 03993-05)

Saliva has a major influence on the acid/base and oxidative metabolisms of the mixed bacteria of saliva and dental plaque. The main objective of our research is to develop an understanding of how saliva and its nitrogenous components, particularly its peptides and proteins, regulate and modify the metabolism and growth of the mixed bacterial populations found in the human oral cavity. Sialin, an arginine peptide discovered earlier in our laboratory is mainly responsible for the pH-rise activity of saliva and may be an agent useful in the control of dental caries. Therefore, the metabolism of Sialin by the oral microflora will be studied using Sialin labelled with 14C using a variety of biochemical techniques. The effect of Sialin on various parameters of carbohydrate and urea metabolism by the mixed oral bacteria will be determined. The arginine polypeptides present in whole saliva will be tested as possible precursors of Sialin. Using similar techniques, the pH-rise activity of pure cultures of oral microorganisms will be examined. Other salivary peptides will be isolated, identified, and tested as oxidizable substrates for the mixed bacteria of saliva and dental plaque. Degradation of salivary proteins and polypeptides by the oral bacteria into small peptides and amino acids will be determined. Their effects on the acid/base and oxidative metabolisms of the mixed oral flora will be examined. The influence of pH, saliva, and salivary peptides on the microbial composition of the salivary and dental plaque microfloras will be examined in vitro.

BIBLIOGRAPHIC REFERENCES: Chatterjee, R. and Kleinberg, I. 1979. Aggregation of salivary proteins. In 'Saliva and Dental Caries'. Information Retrieval, Inc., Washington and London. In press. Globerman, D.Y. and Kleinberg, I. 1979. Intra-oral PO2 and its relation to bacterial accumulation on the oral tissues. In 'Saliva and Dental Caries'. Information Retrieval, Inc. Washington and London. In press.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$146,345

1.0145, INTRACELLULAR CALCIUM METABOLISM IN SALIVARY GLANDS

J.C. Kusek, University of Illinois, Medical Center at Chicago, School of Basic Medical Sciences, Dept. of Pharmacol, *1853 W. Polk St., Chicago, Illinois* 60680 (R01 DE 04081-03)

The object of the proposed research project is to study the role of calcium in the secretory process of salivary glands. The in situ characteristics of calcium influx and efflux during rest and secretion will be determined by Ca45 perfusion studies, and the kinetic parameters of calcium movement will be correlated with various parameters of the salivary secretion. Calcium-45 labeling studies will be used to follow the intracellular movement of calcium during rest and secretion. The subcellular organelles responsible for sequestration and release of that fraction of the total gland calcium which is associated with secretion will be identified, and the subcellular origin of the centrifugal fractions will be determined by enzymatic markers. The characteristics of the calcium sequestering and the calcium-releasing organelles will be determined in vitro using the Ca45-millipore filtration technique. The kinetics and mechanisms of sequestration and release and the effects of pharmacologic agents known to affect salivary gland function will be studied.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0146, PEROXIDASE IN SALIVA AND PREVENTION OF ORAL DISEASE

E.L. Thomas, St. Jude Childrens Research Hospital, Dept. of Biochemistry, *332 N. Lauderdale St., P.O. Box 318, Memphis, Tennessee* 38101 (R01 DE 04235-04)

Lactoperoxidase, hydrogen peroxide and thiocyanate ion form a bacteriostatic system in saliva. The peroxidase-catalyzed oxidation of thiocyanate yeilds hypothiocyanite anion. This antibacterial agent oxidizes a portion of the sulfhydryl components of bacteria, causing inhibition of essential functions and inhibition of growth. However, bacteria can recover from this limited oxidation of sylfhydryls.

The inhibition of bacterial functions by the peroxidase system and the mechanism of recovery will be investigated, using the cariogenic organism, Streptococcus mutans. It will be determined whether the peroxidase system inhibits functions that may contribute to the cariogenic activity of S. mutans, including extracellular dextran synthesis, dextran-induced aggregation and lactic acid excretion. Also these studies will identify the bacterial functions that are not inhibited and which contribute to the recovery process. The experiments will be carried out using purified components and in saliva, so as to determine whether other components of saliva modify peroxidase action, and whether components of saliva are chemically modified by hypothiocyanite. These studies should help to assess the importance of the peroxidase system in saliva, and establish a rational basis for increasing the antibacterial action by blocking recovery.

The location of oxidized sulfhydryls within the bacteria will be determined to evaluate the hypothesis that the limited oxidation of bacterial components is due to the inability of hypothiocyanite ion to penetrate the bacterial cell envelope. Two approaches will be taken to increasing the access of hypothiocyanite to intracellular components: 1. increasing the permeability of the cell envelope, and 2. chemically modifying the hypothiocyanite ion to produce a membrane-soluble oxidizing agent. The objectives are to increase the efficacy or selectivity of peroxidase antibacterial action in ways that will be relevant to the oral environment. In addition, these studies will determine which of the chemical assays for peroxidase action may have value as clinical tests for antimicrobial activity and microbial susceptibility in saliva.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$57,732

1.0147, HUMAN SALIVA - STREPTOCOCCAL METABOLIC INTERACTIONS

R.A. Cowman, University of Miami, School of Medicine, Dept. of Microbiology, *1400 N.W. 10th Ave., Box 520875, Coral Gables, Florida* 33152 (R01 DE 04278-04A1)

This research project is concerned with the metabolic and ecologic interrelationships between oral microorganisms and salivary proteins. Its purpose is to extend earlier observations suggesting that organisms, such as Streptococcus mutans and Streptococcus sanguis, can obtain amino acids required for growth by attacking specific salivary proteins. This evidence was based on non-definitive criteria, namely, changes in the electrophoretic profile of saliva proteins following growth, and concomitant disappearance of amino acids from the total saliva protein concentrate. In order to substantiate these findings it is now proposed: (1) to isolate and characterize specific saliva proteins thought to be susceptible to attack by oral streptococci, (2) to isolate and characterize the microbial proteolytic enzymes involved, and (3) to test the puified protein both as substrates for growth of the streptococci and as substrates for proteolytic enzymes isolated from these organisms. It is further proposed to study the distribution of proteins in the individual salivary gland secretions, from caries-active and caries-free individuals, which are susceptible to proteolytic attack by specific oral streptococci. It is expected that these investigations in a previously unexplored area of dental research will provide new information on host associated factors which influence oral microbial ecology in general, and that this information may also be applicable to the specific problem of individual resistance or susceptiblity to dental caries in humans.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$59,184

1.0148, LYSOZYME-CELL SURFACE INTERACTIONS AND ORAL DEFENSE

J.J. Pollock, State University of New York, Health Science Center at Stony Brook, School of Dentistry, Dept. of Oral Biology & Pathology, *Stony Brook, New York* 11790 (R01 DE 04296-05)

The elucidation of how lysozyme exerts its muramidase, 'lectin-like', cationic and hydrophobic effects to fulfil its biological role in host defense is the main objective of our research. Through an in-depth in vitro investigation of lysozyme's bacteriolytic, bactericidal and bacterial aggregating properties, a better understanding of lysozyme's in vivo antibacterial role should emerge. Since the microbicidal activity of lysozyme may be dependent upon mechanisms similar to those reported for leukocyte cationic proteins, this proposal will examine the virtually unexplored antibacterial effects of parotid salivary cationic proteins. Cationic proteins and other salivary components will be tested in conjunction with lysozyme for potential synergistic antibacterial effects. An understanding of how lysozyme may function in the immune response will be achieved through studies of the interaction of lysozyme with human mononuclear cells. Screening techniques for the identification of lysozyme receptors will be developed and receptors on bacterial and mammalian cells will be isolated and characterized. The molecular nature of the interaction of the purified receptors with lysozyme will also be investigated. Such studies will be of particular significance since several of these bacterial receptors have been implicated in the pathogenesis of dental caries and periodontal disease. Using similar screening procedures, the lysozyme binding components of parotid saliva will be isolated and characterized. A radioimmunoassay for parotid lysozyme will be developed for quantitation of true concentrations of lysozyme in freshly isolated and fractionated human parotid saliva.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $131,321

1.0149, SALIVARY LACTOFERRIN AND REGULATION OF THE ORAL FLORA

R.R. Arnold, University of Alabama in Birmingham, School of Medicine, Dept. of Microbiology, *1919 7th Ave. S., Birmingham, Alabama* 35233 (R01 DE 04801-03)

Lactoferrin (LF) is an iron-binding protein synthesized by neutrophils and glandular epithelial cells. LF has been detected in most of the major secretions that bathe human mucosal surfaces; including saliva. Previous studies have indicated that LF can reversibly inhibit the growth of a variety of microorganisms by binding available iron making it inaccessible to the bacteria. This inhibition is readily reversed by the addition of exogenous iron. Recent studies in our laboratory have indicated that LF is capable of a direct irreversible inhibition of certain bacteria. This bactericidal effect is dependent on the chelating properties of LF. A survey of microorganisms indicated that a number of oral microorganisms was susceptible to the bactericidal activity of LF, suggesting a potentially potent mechanism of the regulation of the oral flora by salivary LF. Bacterial resistance to LF appears to be associated with the virulence of the organism. Current studies are being directed at the kinetics of action of LF and assessing the effects of LF on various bacterial components. Through such studies it might be possible to determine the mechanism of bacterial resistance and indirectly the mode of LF action. Possible interactions between LF and other salivary components such as antibody, lysozyme, and lactoperoxidase are also being investigated with either purified components or in saliva from various immune deficient and control subjects. The in situ effects of LF in dental plaque and plaque free-fluid by quantitation and analysis of localization of LF. The effects of LF on colonization, metabolism and macromolecular synthesis of various oral microorganisms are being evaluated in in vitro systems.

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SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $50,049

1.0150, REMINERALIZATION OF ENAMEL CARIES IN VITRO

L.M. Silverstone, University of Iowa, School of Dentistry, Dept. of Pedodontics, *Jessup Hall, Iowa City, Iowa* 52240 (R01 DE 04819-03)

Remineralization of Enamel Caries: After exposure to a CF, lesions appear to be at a very much earlier stage than prior to experiment. When the CF contains a low calcium level (1 mM) changes are produced throughout the entire depth of a lesion. When higher calcium concentrations are used (3mM) remineralization occurs but it is limited to just the surface of the lesion. The CV contains a low concentration of fluoride. How does this compare to using a fluoride solution alone? Exposure of a lesion to fluoride alone does not alter the size or porosity of the lesion. However, exposure to a CF containing only 1ppm fluoride produces a significant reduction in a lesion with respect to both depth and porosity.

Effect of Remineralization on Lesion Progression: How does remineralization effect the progress of an established lesion when another cariogenic challenge occurs? For this investigation, the artificial caries technique is used to create small caries-like lesions in enamel. A control section is removed to establish the size of the lesion, and then one half of the lesion is exposed to the CF while the control half is exposed to deionized water. After a suitable exposure time, a section is removed from the test half to determine the degree of remineralization produced. After this both the test and control halves of each lesion are returned to the artificial caries system. Results to date show that the remineralized half of the lesion is far more resistant to progression compared to the control half of the same lesion. In terms of remineralization of a static lesion (Part A), the CF with a low calcium level was most effective since it remineralized the lesion in depth. With a higher calcium level, only the surface of the lesion was remineralized. However, with respect to lesion progression, the CF with high calcium was at least as effective in retarding lesion progression.

BIBLIOGRAPHIC REFERENCES: SILVERSTONE, L.M., ZIMMERMAN, B.F., KASTENDIECK, M.J., WEFEL, J.S., AND CLARKSON, B.H. 1979 Progression of caries-like lesions in vitro after exposure to synthetic calcifying fluids, J. Dent. Res. 58, Special Issue A: 283. ZIMMERMAN, B.F., SILVERSTONE, L.M., CLARKSON, B.H., WEFEL, J.S. AND KASTENDIECK, M. 1979 The effect of remineralization fluids on carious lesions in vitro. J. Dent. Res. 58, Special Issue A: 282.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$101,716

1.0151, PROTEIN INHIBITORS OF CALCIUM PHOSPHATE PRECIPITATION

D.H. Schlesinger, University of Illinois, Medical Center at Chicago, School of Basic Medical Sciences, Dept. of Physiology, *1853 W. Polk St., Chicago, Illinois* 60680 (R01 DE 05059-02)

During the first year of the proposed project, we have embarked upon the structure elucidation of protein and peptide inhibitors of calcium phosphate precipitation in human saliva as well as saliva of other species. To date we have completed the primary structure of statherin and most potent, and smallest, of the four anionic proline-rich proteins (PRP) in human saliva and have begun sequence determination of the protein inhibitors of calcium phosphate precipitation in saliva of other species as a first step comparative structural studies. An anionic proline-rich (PRP-like) protein and a statherin-like peptide from saliva of Macaca Arctoides have been highly purified. We have carried out NH2-terminal sequence analysis and have purified and partially sequenced the maleoylated tryptic peptides of the PRP-like protein from Macaca Arctoides, and we are presently initiating structural analysis on the statherin-like peptide. Finally we have extended our comparative structural studies by looking for inhibitors of calcium phosphate precipitation in the saliva of venomous and non-venomous snakes and other species phylogenetically distant from man.

In addition to these comparative structural studies, we have begun localizing the site of precipitation-inhibition in the salivary phosphoproteins. We have demonstrated that the NH2-terminal tryptic peptides of all four anionic proline-rich proteins from human saliva contain the active regions necessary for calcium phosphate precipitation-inhibition and have purified and characterized on active collaginase fragment of statherin. Presently we are beginning synthetic studies to accurately define the active regions of these molecules and to determine minimal peptide chain lengths required for activity.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$60,698

1.0152, SALIVARY IMMUNE FACTORS

S.A. Ellison, Columbia University, School of Dental & Oral Surgery, Dept. of Oral Biology, *Broadway & W. 116th St., New York, New York* 10027 (R01 DE 05531-01)

Currently used assays for salivary antibacterial systems will be surveyed; novel tests, readily related to clinical studies will be developed. Biological assays will be compared with immunochemical ones. The antibacterial effectiveness of lactoferrin, lactoperoxidase, and lysozyme, alone and in concert, will thus be gauged. Clinical studies will include comparison of caries-resistant and caries susceptible persons, determination of changes associated with aging, and examination of secretions from persons with parotitis. Concurrent microbiological studies will be done to relate saliva content of these factors to alterations or differences in the oral bacterial population.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $117,269

1.0153, WORKSHOP ON SALVIA AND DENTAL CARIES

I. Kleinberg, State University of New York, Health Science Center at Stony Brook, School of Dentistry, Dept. of Oral Biology & Pathology, *Stony Brook, New York* 11790 (R13 DE 04984-01)

This symposium has several objectives. These include determination of the current status of studies on saliva in relation to caries research; identification of new areas for investigation and areas that need to be reexamined; critical evaluation of the methodology and the various model systems currently being used in salivary caries research; stimulation of researchers within and outside of dentistry to focus on key problems; examination of saliva as a vehicle for, and an antagonist to, the use of chemotherapeutic agents for the prevention of dental caries; publication of the information gathered at this workshop in monograph form and making it available for general use.

To accomplish these objectives, the proposed symposium will bring together persons of diverse backgrounds and interests from dental research and other disciplines. Presentations and discussions have been organized along the following lines. The first group of papers will deal with the nature of the constituents of the salivary secretions. Because of their importance, emphasis will be placed on the various classes of salivary proteins, as well as the effects of a variety of physiological and pathological factors on their secretion. The second group of presentations and discussions will examine the role of saliva in the caries process through its influence and that of its components on the oral bacteria, the carbohydrate available for their utilization and the teeth they attack. The third part will deal with the defense systems common to exocrine secretions and an exploration of the various human, animal, and in vitro models currently being used to study saliva-caries relationships, the problems imposed by saliva when therapeutic agents are used against dental caries and strategies for utilizing salivary secretions in caries prevention. The concluding session of the symposium will provide an opportunity for presentation and discussion of recommendations for future research prepared by assigned task groups.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0154, SALIVARY PROTEINS IN BACTERIAL AGGREGATION/ADHERENCE

V.W. Ryan, Stevens Inst. of Technology, School of Engineering, Dept. of Physics, *Castle Point Station, Hoboken, New Jersey* 07030 (R23 DE 05436-01)

The interactions among salivary components, oral bacteria, and enamel surfaces are processes which are important for the initiation of a carious lesion. This study, an extension of our earlier work on dextran, proposes to focus on those salivary proteins which are capable of binding both hydroxyapatite and Streptococcus mutans. We plan to test quantitatively the protein bridge model for bacterial aggregation and also for Cellular adherence to a hydroxyapatite substrate. The technique of quasielastic laser light scattering will be used to determine the physical characteristics of the saliva fractions, the aggregation rates of the bacteria, and the concentration of bacteria that is bound to hydroxyapatite under different conditions including fluoride treatments. The specificity of the S. Mutans protein binding sites will be examined as well as the relationships between the protein characteristics and the effectiveness of the bridging mechanism.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $23,300

1.0155, SPECIFIC AND NON-SPECIFIC IMMUNE FACTORS IN PLAQUE FLUID AND SALIVA

M.F. Cole, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Preventive Methods Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00222-03 CPR)

The free aqueous phase was obtained from individual samples of dental plaque and the plaque matrix was then eluted at low pH in an attempt to remove bound protein. The fluid and the low pH phases were assayed for secretory immunoglobulin A (SIgA), IgG, IgM, the third component of complement (C'3), lysozyme, lactoperoxidase and lactoferrin. The presence of these specific and nonspecific immune factors in the free and bound phases suggest they are important in host defense at the plaque-enamel interface.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $12,970

1.0156, RADIATION CARIES IN PRIMATES

W.M. Edgar, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00231-03 CPR)

Plaque fluid and saliva samples from 4 irradiated monkeys (Macaca mulatta) and from groups of non-irradiated controls, all receiving a cariogenic diet, were analyzed on an individual basis for inorganic and organic constituents. Basic information on the composition of plaque fluid from animals with contrasting caries and on the effects of salivary gland irradiation is accumulating, giving some insights which may be relevant to caries in man.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $30,787

1.0157, INDUCTION OF SECRETORY IMMUNITY IN THE GNOTOBIOTIC RAT

M.F. Cole, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Preventive Methods Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00235-02 CPR)

Germ free rats were immunized orally, intragastrically and intramucosally with Streptococcus mutans 6715-15. Unimmunized animals served as controls. All rats were infected with S. mutans 6715-15. After 8 weeks the rats were sacrificed and serum, saliva, gut and pulmonary washes were collected. In addition, splenic, salivary, mesenteric and Peyer's Patch lymphocytes were assayed. Serum and salivary antibodies were detected in all groups. Primed lymphocytes were detected in spleen and salivary lymph nodes.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $6,683

1.0158, IMMUNOGLOBULINS AND ANTIBODIES IN PLAQUE FLUID AND SALIVA IN TWO POPULATIONS WITH CONTRASTING LEVELS OF CARIES

M.F. Cole, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Preventive Methods Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00237-02 CPR)

Plaque fluid and saliva were collected from 25 children aged 7-12 years from two communities with contrasting levels of caries and assayed for secretory immunoglobulin A (SIgA), IgG, IgM, complement (C'3) and lysozyme. Significantly more IgA was found in the saliva and lysozyme in the plaque fluid from subjects with low caries experience. Subjects exhibiting antibody reactive with S. mutans serotypes a and d had a lower prevalence of caries than those who failed to demonstrate antibodies.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $27,322

1.0159, PASSIVE IMMUNITY AGAINST DENTAL CARIES IN THE RAT

M.F. Cole, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Preventive Methods Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00258-01 CPR)

Antiserum against formalin killed whole cells of Streptococcus mutans was raised in rabbits. The antiserum was added to the drinking water of one group of weanling conventional Osborne Mendel rats. Their controls received drinking water containing non-immune rabbit serum. Five days after the initiation of passive immunization all animals were infected with the homologous S. mutans strain. After 8 weeks the experiment was terminated, the teeth scored for caries and the numbers of S. mutans determined. There was a significant reduction in the number of S. mutans in the immunized group however, no significant difference was detected in the level of caries. This probably resulted from the high level of non-S. mutans background caries activity seen in these animals.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $26,061

1.0160, ROLE OF HOST SALIVA ON IMPLANTATION OF S. MUTANS IN HUMAN DENTAL PLAQUE

J.E. Ciardi, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00274-01 CPR)

The ability of exogenous S. mutans to implant and be retained in dental plaque varies considerably among human subjects. Because of differences in susceptibility to implantation by S. mutans, test subjects were divided into three groups: 1) Highly susceptible; 2) Moderately susceptible; and 3) Not susceptible. The purpose of the present investigation is to determine if a significant correlation exists between host saliva and S. mutans implantation by initially assessing the effects of these salivas on bacterial growth, acid production, aggregation, and ability to adhere to surfaces - all activities involved in the caries process. Results will be compared with respect to the three test groups.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $4,717

1.0161, ETIOLOGY AND CONTROL OF ORAL DISEASES

R.J. Fitzgerald, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Oral Microbiology Laboratory, *1201 Northwest 16th St., Miami, Florida* 33125 (546-001-P)

This research program aims (1) to identify organisms of etiological significance in dental caries, (2) to determine the biological determinants of cariogenesis and (3) to apply this knowledge to control of caries. Previous reports have described the ability of all strains of Streptococcus mutans regardless of type or source to induce caries in experimental animals and the limited cariogenicity of other dental plaque streptococci. We have now found that certain oral strains of Lactobacillus salivarius and Lactobacillus fermentum can induce caries in conventionally reared hamsters and in germfree rats. Although these lactobacilli produce acids from carbohydrates they do not possess certain other traits which have been associated with cariogenicity in S. mutans, namely production of extracellular polyglucan, synthesis of intracellular amylopectins and ability to form tenacious deposits in vitro on extracted teeth. Efforts are now underway to determine the mechanisms responsible for the cariogenicity of these lactobacilli since caries control measures directed against S. mutans may not be effective against cariogenic lactobacilli. In other studies we have found that certain salivary glycoproteins from caries-active individuals are selectively adsorbed to hydroxyapatite, (HA), the prinicipal enamel mineral. As a group these proteins can be readily utilized as nitrogenous growth substrates by S. mutans but much less efficiently by other oral streptococci. Because of the potential significance of this phenomenon as a selective virulence determinant for S. mutans in dental caries we are now in the process of isolating individual proteins from caries-active and caries-free individuals to determine if differences in their affinity for HA and utilization by S. mutans are relatable to differences in caries susceptibility.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

1.0162, ROLE OF SALIVARY AND DIETARY FACTORS IN XEROSTOMIA-INDUCED DENTAL CARIES

R.A. Cowman, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *1201 Northwest 16th St., Miami, Florida* 33125 (546-002-I)

This research seeks to clarify the role of the salivary nitrogenous constituents as a contributory factor in the development of rampant dental caries in patients who have undergone radiation therapy for head or neck carcinomas by: (1) examining the extent to which the salivary protein composition of mixed saliva and the individual glandular secretions is altered following direct irradiation of the major salivary glands, and (2) ascertaining the effect of such changes on the activity of the salivas supporting the growth of Streptococcus mutans and other plaque-associated oral streptococci. Citric acid-stimulated whole saliva was obtained from patients at pre-treatment, at weekly intervals during treatment, and monthly thereafter. Individual glandular secretions also were obtained when possible. Analytic tests included isoelectric focusing to establish constituent protein patterns and microbial growth tests. Mixed salivas from 2 patients have been examined in some detail. Electrophoretic studies indicated that major changes in protein composition occurred within the first 3 weeks of therapy. Amylase, the major salivary protein, rapidly disappears and there is a shift to a composition predominated by proteins having isoelectric points below pH 5.60. The change in salivary protein composition does not appear to adversely affect the growth supportive activity of the salivas for S. mutans, however, S. sanguis exhibits a continually lessened ability to utilize the salivas as nitrogenous growth substrates. We therefore intend to further characterize the changes occurring in salivas from our patient population and to evaluate the relevance of these alterations as a contributory factor in onset of rampant caries in patients with radiation-induced xerostomia.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

ETIOLOGY - DIET

1.0163, THE EFFECT OF PROTEIN MALNUTRITION ON DENTAL CARIES AND SALIVARY GLAND PROTEIN SYNTHESIS

L. Menaker, University of Alabama in Birmingham, School of Dentistry, Dept. of Nutritional Sciences, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130017)

The specific role of protein malnutrition, during gestation and lactation periods, in the etiology of dental caries is under investigation. In addition, the interaction of protein malnutrition and fluoride supplementation, as well as the interaction of fluoride and sucrose, are under study in an attempt to develop new vehicles for caries preventive agents. Furthermore, the effect of protein malnutrition on the biochemistry of the salivary glands and the protein content of the saliva is also a topic being studied, with an effort made to understand the interrelationships between salivary changes and disease conditions.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$54,608

1.0164, NUTRITIONIONAL STUDIES ON GROWTH, DEVELOPMENT, AND SUSCEPTIBILITY TO DISEASE OF ORAL TISSUES

J.M. Navia, University of Alabama in Birmingham, School of Dentistry, Dept. of Comparative Medicine/Biochemistry/Nutritional Scien, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130020)

The primary objective of this research program is to investigate the effects of nutrients and foods on growth, development, and maintenance of oral tissues, as well as their influence on oral diseases such as dental caries. Major research topics include: (1) Development of animal models and procedures to be used in dental caries research: identification of sources of variability. (2) Studies of the nutritional factors affecting the metabolism and cariostatic properties of fluoride and other trace elements. (3) Studies related to the effects of marginal protein-calorie malnutrition or vitamin A deficiency on growth and development of bones and teeth. (4) Study of bone metabolism and metabolic bone disease (osteoporosis) with particular emphasis on zinc, calcium, phosphorus, fluoride, vitamin C and protein, and their possible metabolic interactions.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$174,833

1.0165, ZINC DEFICIENCY AND DENTAL CARIES

N.R. Calhoun, Howard University, School of Dentistry, Dept. of Oral Surgery, *2400 6th St. N.W., Washington, District of Columbia* 20001 (R01 DE 04760-02)

We will repeat our study of the pre-eruptive influences of a zinc deficiency of subsequent dental caries susceptibility. After delivery, female rats and their suckling pups will be divided into four groups. zinc deficient group will be fed a diet containing a maintenance level of zinc. The zinc sufficient group will receive a diet high in zinc. The pair fed group will be fed an amount of the zinc sufficient diet equal in amount to the intake of the zinc deficient group. A supplemented group will be fed the zinc deficient diet plus a supplement of zinc to maintain weights and plasma zinc levels similar to the zinc sufficient group. At weaning, the pups will be fed a cariogenic diet and after 5-6 weeks scored for dental caries.

Then we will continue with studies to determine why the zinc deficiency is influencing caries susceptibility. We will examine the microflora changes with diet, eruption time of the molars, tooth histology and saliva composition alterations.

Also, we will examine post-eruptive influences of zinc deficiency. Rats will be fed a zinc deficient cariogenic diet beginning at weaning and then scored for caries. This group will be compared with ad libitum and pair fed groups receiving the cariogenic diet with adequate zinc.

SUPPORTED BY
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $0

1.0166, EFFECT OF EATING PATTERNS ON DENTAL CARIES IN RODENTS

W.M. Edgar, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00268-01 CPR)

Human studies have indicated the importance of food sequence in pH changes in dental plaque in situ. This concept has been extended by feeding rats according to a programmed sequence of foods, interspersing foods of low potential cariogenicity (peanuts, cheese) between exposures to cariogenic diet. With cheese (but not peanuts) caries and Strep. mutans counts were reduced compared with controls fed cariogenic diet alone, in partial agreement with the human studies.

SUPPORTED BY
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $11,079

1.0167, INVESTIGATION OF INFANT AND PRESCHOOL DIETS AND THEIR RELATIONSHIP TO DENTAL HEALTH

G.D. Derkson, University of British Columbia, Faculty of Dentistry, *2075 Wesbrook Pl., Vancouver, British Columbia, Canada* V6T 1W5

PURPOSE: To determine the incidence of nursing bottle syndrome (deep carious lesions in the upper primary incisors and the upper and lower primary first molars) in Vancouver preschool children; and to examine their health and diet histories to determine what factors might correlate with the incidence of the disease.

SUBJECTS: As many preschool children as possible, ages 9 months to 5 years, of either sex, secured from the records of the Vancouver Health Department and child health centers.

METHODS: Mothers consenting to participate will be interviewed as to the health and dietary history of their children in order to complete a detailed questionnaire. The child's teeth will be examined, using a mouth mirror and flashlight, to determine whether or not the child exhibits the typical lesions of nursing bottle caries.

SUPPORTED BY
(No Supporting Organization Reported) funds n.a.

1.0168, ORAL CONDITIONS IN RELATION TO TRACE ELEMENTS IN HUMAN TISSUE AND THE ENVIRONMENT

P.M. James, University of Birmingham, Dept. of Dental Health, *P.O. Box 363, Birmingham, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY
Medical Research Council $3,585

1.0169, CARIOGENICITY OF XYLITOL, MANNITOL, SORBITOL AND SUCROSE

K. Shyu, National Defense Medical Center, Dept. of Dentistry, *P.O. Box 8244, Taipei, Taiwan, Republic of China* (NSC-68B-0412-06-12)

Direct replacement of sucrose with other natural and less cariogenic dietary sugars in foodstuffs and other products is one of the best methods of caries prevention. In this study, three low cariogenic sweeteners, xylitol, mannitol and sorbitol, will be used to replace sucrose in the diet for Sprague-Dawley rats. Diets with or without sucrose will be used for control groups. Half of the animals of each group will be sacrificed after 50 and 100 days of feeding. Immediately after sacrifice, the mandible of each rat will be dissected, cleaned, fixed, stained and examined under microscope. Dental caries will be scored following Keyes' method. The least cariogenic sugar, probably xylitol, will be used in my next experiment to find out the optimal percentage of replacement for sucrose, with lowest cariogenicity and least side effect, if any. This least cariogenic sweetener will be adopted in a human experiment to replace sucrose in optimal percentage. If the result is satisfactory, it will be recommended to be used as substitute for part of the dietary sucrose to prevent dental caries.

SUPPORTED BY
National Science Council $3,303

1.0170, EFFECTS OF B6 AVITAMINOSIS ON THE GROWTH AND THE DEVELOPMENT OF BUCCO-DENTAL STRUCTURES OF THE RAT

J.C. Franquin, Universite dAix Marseille, Faculte de Chirurgie Dentaire, Dept. of Biology & Fundamental Materials, *Charles Livon Blvd., Jardin Emile Duclaux, 13007 Marseille, France*

Carried out in collaboration with the Cancer Research Institute, this project aims at the study, under very precise dietary conditions, of the effects of B6 avitaminosis on growth and development of the buccotdental structures of the white rat.

The first part of this project which is being carried out at present, consists of a histologic study of the disturbances observed at the level of the dental germs, the ossification centers of the skull base, and the condyle of the 21-day old fetuses after maternal deprivation.

The second part of this project includes, on the one hand a histological study of these same buccodental structures of the weaning young rat, and on the other hand a qualitative and quantitative microradiographic study of the mineralization variations of the calcified dental tissues.

The third part of this project covers the disturbances which may occur with the adult rat.

The results obtained with the first part of this study have been presented at the Rome Congress of the I.A.D.R. in June 1977.

SUPPORTED BY

Universite dAix Marseille	funds n.a.

ETIOLOGY - MICROBIAL FERMENTATION

1.0171, VIRULENCE CHARACTERIZATION IN STREPTOCOCCUS MUTANS

J.M. Tanzer, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Oral Diagnosis, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 03758-05)

The long-term objective of research is the identification of the genetic and biochemical determinants of virulence (virulence factors) of Streptococcus mutans, their characterization and the estimation of the efficacy of some cell-surface associated virulence factors as antigens against which immunization may be directed. Using bacteriological, biochemical, immunological and experimental pathology procedures work will be directed at further characterization of glucosyl transferases, glucan linkage patterns, glucan binding sites, glucanohydrolase activity, and other virulence-associated properties of WT organisms and mutants of them defective in those selected traits. Studies will explore the role of these traits in virulence expression and their possible utility in experimental protection of animals against dental caries.

BIBLIOGRAPHIC REFERENCES: Tinanoff, N. and J.M. Tanzer. Bacterial pellicle-like substances and polyphosphate formation by enamel-adherent oral microorganisms. J. Pediat. Dent. 1:1-5, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$107,809

1.0172, UPTAKE OF HYDROXYAPATITE PHOSPHORUS BY ORAL BACTERIA

F.E. Shovlin, College of Medicine & Dentistry of New Jersey, New Jersey Dental School, School of Dentistry, Dept. of Oral Biology, *100 Bergen St., Newark, New Jersey* 07103 (R01 DE 03867-06)

The utilization of phosphate ions from hydroxyapatite by oral bacteria may be significant in the carious process. Dual labeling of extracted teeth by means of neutron-irradiation (45Ca and 32P) provides a method for studying the fate of these ions in an in vitro system.

To date, an isolate from deep dentinal caries (L. casei) that stores intracellular polyphosphate (polyP) granules has been used as a prototype for these studies. It has been determined that the organism utilized significant amounts of hydroxyapatite which is incorporated predominantly into the nucleic acid and polyP fractions. The calcium ions are also utilized by the bacteria and may appear in the polyP fraction. Calcium ion concentration is also high in the supernatant fluid when compared with phosphate in the same fraction.

In proposed studies, the disposition of the calcium ions will be better defined by isolation of bacterial cell fractions using milder procedures. In addition, the effects of inhibition of polyP formation on the uptake of hydroxyapatite phosphate will be determined. Inhibition of this fraction may play a significant role in decreasing hydroxyapatite dissolution since approximately 50% of the cell phosphate is found in the polyP fraction and furthermore this fraction can be synthesized in the absence of cell growth.

The methods of procedure developed with the prototype organism will be used to study the disposition of calcium and phosphate ions in cultures of Strep. mutans and actinomyces species described as cariogenic by other laboratories.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$70,441

1.0173, THE ROLE OF BACTERIAL METABOLITES IN ORAL DISEASES

R.A. Pieringer, Temple University, School of Medicine, Dept. of Biochemistry, *3322 Broad St., Philadelphia, Pennsylvania* 19122 (R01 DE 04957-01A1)

Membrane lipoteichoic acids (LTA) are synthesized and excreted by variety of oral bacteria. We shall study the structure, metabolism, excretion, function and control of the metabolism of LTA in these organisms. The LTA's which have been strongly implicated in a number of oral diseases are synthesized by enzymatic reactions that do not occur in animal tissues. This metabolic difference offers the possibility of a new chemotherapeutic approach to oral disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$58,037

1.0174, COMPOSITION OF S. MUTANS IN DIFFERENT GROWTH ENVIRONMENT

L. Daneo Moore, Temple University, School of Medicine, Dept. of Microbiology & Immunology, *3322 Broad St., Philadelphia, Pennsylvania* 19122 (R01 DE 05180-01)

A novel mathematical approach using matrix analysis will be applied to study the effects of the environment of oral bacteria on their macromolecular composition. The proposed study emphasizes determinations of surface composition, intracellular polysaccharide content, intracellular nucleotide pools and quantitation of several excreted macromolecules. From this study should emerge a profile of those environmental conditions that are most advantageous, as well as deleterious to colonization, pathogenicity and immunogenicity of oral streptococci.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$52,823

1.0175, COMPARATIVE PHYSIOLOGY OF LACTIC ACID BACTERIA AND OTHER ORAL MICROBES

J. London, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Microbiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00022-13 LMI B)

For summary: see 2.0024.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$33,094

ETIOLOGY - MISCELLANEOUS

1.0176, PRIMATE MODEL FOR DENTAL CARIES STUDIES

D.W. Dalgard, Hazleton Lab. America Inc., *9200 Leesburg Tpke., Vienna, Virginia* 22180 (N01DE52458 (CONTRACT))

The Contractor proposes to develop an animal model for the study of dental caries in the new world species, namely, the Saimirc sciureus species. Emphasis will be placed on designing a method which will induce caries rapidly and yet one in which the results will be applicable to the human disease. In addition to studying caries susceptibility in the feral-reared imported animal, breeding groups will be established to enable studies in the domestically reared infants.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0177, MECHANISM OF HARD TISSUE MINERALIZATION

A.L. Boskey, Hospital for Special Surgery, Dept. of Biochemistry, *535 E. 70th St., New York, New York* 10021 (R01 DE 04141-05)

Calcium-acidic phospholipid-phosphate complexes have been associated with the initiation of in vitro and in vivo mineralization (e.g., endochondral ossification). The distribution of such complexes in normal (developing dentin, fracture callus) and abnormal calcifications (osteoarthritic osteophytes, necrotic bone, salivary stones) is being studied. Factors which control lipid-induced calcification from solution include pH, Ca and PO4 concentration, the presence of calcification inhibitors, the presence of surfactants (such as the lysophosphatides), and the presence of specific enzymes. The precise role of phospholipase A2, (an enzyme whose activity increases in the epiphyseal growth plate prior to calcification), in lipid induced calcification is being studied by determining the effects of the enzyme on the kinetics of in vitro hydroxyapatite formation. The role of Mg, pH, and other controlling factors is being evaluated in similar kinetic experiments.

BIBLIOGRAPHIC REFERENCES: Boskey, A.L., Goldberg, M.R., Lane, J.M. and Posner, A.S., The calcium-phospholipid-phosphate complexes associated with mineralizing tissues: In vivo and in vitro studies. Orthopaedic Trans. 2, No. 1, 134-135, 1978. Boskey, A.L., Lackman, R.H., Cordella, D.M., Lane, J.M. and Posner, A.S., Ca-Phospholipid-PO4 Complexes in Endochondral Calcification: Growth Plate Zones and Fracture Callus. Orthopaedic Trans. 2, No. 1, 135, 1978.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $32,353

1.0178, LABORATORY AUTOMATION OPTIMIZATION OF COMPUTER RESOURCES IN DENTAL RESEARCH

T.P. Medlin, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Scientific Systems Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00030-12 OD)

The utilization of computers as a research tool is well known. The mixture of computers in a distributed processing scheme is gradually gaining acceptance. Other issues are what mixture of computer peripherals and what types of software yield the best long-term results in a research environment. The goal of this project is to review the needs of researchers and map these needs into the best system of computers, peripherals, and software in an optimal way.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $146,575

1.0179, DEVELOPMENT OF AN IMAGE PROCESSING FACILITY FOR DENTAL RESEARCH

T.P. Medlin, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Scientific Systems Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00265-01 OD)

The use of dental radiographs as a diagnostic tool in a clinical regimen is well known. The information provided by a radiograph can be enhanced by appropriate filtering, smoothing, and enhancement via standard image processing techniques. Blending in video techniques and equipment with analog options and digital computers to provide an optimal environment for continued research is the aim of this project.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $9,739

PATHOLOGY

1.0180, EVALUATE PEPTIDES AS CHEMOATTRACTANTS FOR LEUCOCYTES

R.J. Freer, Virginia Commonwealth University, School of Basic Sciences & Graduate Studies, Dept. of Pharmacology, *901 W. Franklin St., Richmond, Virginia* 23284 (N01DE62494 (CONTRACT))

'Evaluation of Small Synthetic Peptides as Chemottractants for Leucocytes and their Application to Periodontal Disease' is a study which will provide for the synthesis of 20 or more formylmethionyl peptides or related compounds per year. The synthetic procedure will involve well-developed methods with few side reactions. The purification of the compounds should be accomplished with simple recrystallization and ion-exchange methods. The compounds then should be tested for chemotactic activity, effects of increasing molecular size, presence or absence of N-acylation, esterification or amidation of carboxyl groups.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $140,191

1.0181, VITAMIN A, FLUORIDE AND GLYCOSAMINOGLYCANS IN BONE

L. Singer, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160080)

For summary: see 2.0192.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $6,800

1.0182, METHODS FOR THE ULTRACYTOCHEMICAL DEMONSTRATION OF ENZYMES AND BIOMACROMOLECULES OF ORO- AND CRANIOFACIAL TISSUE

J.S. Hanker, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Oral

Surgery, *Chapel Hill, North Carolina* 27514 (P50 DE 02668e130196)

For summary: see 2.0071.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$13,192

1.0183, CLINICAL EVALUATION OF RESTORATIVE MATERIALS AND TECHNIQUES

K.F. Leinfelder, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Operative Dentistry, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130197)

The neurobiology of the afferent trigeminal system and the sympathetic and parasympathetic autonomic fibers innervating vascular and glandular structure of the orofacial region will be studied with direct ultracytochemical, immunocytochemical, and glyoxylic acid- or formaldehyde-induced fluorescence methods. The studies will be performed to mechanisms of normal growth and development, and developmental characteristics of disease states or regeneration after surgical interruption.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$21,107

DIAGNOSIS & TREATMENT

1.0184, NAVY ENVIRONMENT - RATIONAL TREATMENT OF DECAYED TEETH IN NAVAL PERSONNEL

K. Langeland, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Materials Science, *Farmington Ave., Farmington, Connecticut* 06032 (N00014-75-C-0758)

The response of the tooth pulp to progressive decay and to clinical procedures used to control it can lead to incapacitating pain which may occur at stations where no dental facilities exist in the case of armed forces personnel. The objective of this investigation is to assure optimum treatment of deep caries and to extend our understanding of the pathological processes involved.

In collaboration with the Naval Dental Research Institute, Great Lakes, Illinois, histological and bacteriological examinations of pulp and dentin are being carried out and correlated with the clinical diagnosis. Observations are made of the effects of different forms of therapy with respect to the subsequent condition of the pulp and dentin after appropriate observation periods.

SUPPORTED BY

U.S. Dept. of Defense, Navy, Office of Naval Research	$33,044

1.0185, SYSTEM FOR EARLY DETECTION OF DENTAL CARIES

G.E. White, Tufts University, Boston Campus, School of Dental Medicine, Dept. of Oral Pediatrics, *136 Harrison Ave., Boston, Massachusetts* 02111 (N01DE52476 (CONTRACT))

'The Development and Evaluation of a Diagnostic System for the Early Detection of Dental Caries'. This is a research and development of a valid clinical method for diagnosing early carious lesions in human teeth. This method will rely on clinical trials for its final evaluation with comparison made on the basis of caries development between groups differentially exposed to the test agent or procedure.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$76,527

1.0186, LUMINESCENCE AND POLARIZED LIGHT IN THE DIAGNOSIS AND TREATMENT OF INCIPIENT CARIES

W.J. O'Brien, University of Michigan, Ann Arbor Campus, School of Dentistry, *Ann Arbor, Michigan* 48104 (P50 DE 02731-130037)

The objective of this study is to develop and evaluate techniques employing luminescence and polarized light in the detection of enamel demineralization. Particular emphasis will be placed upon the detection of incipient caries and the effects of acids applied in the early treatment and prevention of caries: fluoride treatments and sealant application.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$76,538

1.0187, DEVELOPMENT AND EVALUATION OF IMPROVED DENTAL RADIOGRAPHIC

SYSTEMS WITH EMPHASIS ON FACTORS INFLUENCING DIAGNOSTIC PERFORMANCE

R.L. Webber, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Diagnostic Methodology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00065-08 CI)

Factors influencing the clinical performance of dental x-ray systems including a portable dental fluoroscope are being evaluated in vitro using computer simulations and quantitative measurements derived from radiographic phantoms.

Measures of clinical utility based on an endodontic task using dentulous skulls are being determined for various film/screen combinations in order to access the minimum information capacity required. It is anticipated that these findings will aid in establishing the minimum signal-to-noise ratio and resolution characteristics necessary for endodontic radiography.

Other studies based on spectral analyses of 125I and 153Gd using non-linear systems model indicate significant technical limitations which minimize the practicality of such isotopes as x-ray sources in routine dental fluoroscopic applications.

Factors influencing geometric registration of successive radiographic projections are also being explored in an effort to establish a practical means for quantitatively tracing degenerative changes in tissues of dental interest over time.

BIBLIOGRAPHIC REFERENCES: Lieberman, J. E. and Webber, R. L.: Clinical evaluation of prototype intraoral source x-ray system. Oral Surg., Oral Med., Oral Path. 46: No. 2, 318-327, 1978. Yin, L. I., Trombka, J. I., Seltzer, S. M., Webber, R. L., Rennie, J., and Farr, M. R.: The lixiscope. SPIE Conf. Proc. 143: 106-113, 1978.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $35,480

1.0188, ENHANCEMENT OF DIAGNOSTIC IMAGES

R.L. Webber, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Diagnostic Methodology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00211-03 CI)

This project is an extension of previous work involving the creation, development, and testing of image processing techniques designed to improve diagnostic performance. Recent emphasis has centered on position-invariant filtering schemes to eliminate known sources of noise in CAT scans. Other work involves testing of the computer implemented transformation which creates an isometric three-dimensional 'pseudo-solid' from any two-dimensional array of grey levels. Comparisons of processed and controlled images by unbiased observers suggest that diagnostic performance is limited by sample restrictions imposed by a severe angular dependence on the pseudo-solid algorithm when using shadows as cues to depth. Modifications of this and the other promising enhancement schemes reported on last year are being explored to further define factors limiting diagnostic performance.

This project will continue to forgo investigation of empirical enhancement schemes per se in favor of approaches which are based on relatively specific theoretical concepts.

BIBLIOGRAPHIC REFERENCES: Webber, R. L. and Nagel, R. N.: Image preprocessing as an aid to visual interpretation. IADMFR Proc. (1978) (In Press).

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $29,748

1.0189, CARIES, MATERIALS, BACTERIA AND PULP RESPONSE

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No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY
Medical Research Council $15,724

1.0190, IN VIVO AND IN VITRO STUDY OF THE REMINERALIZATION OF CARIOUS DENTINE

J.C. Franquin, Universite dAix Marseille, Faculte de Chirurgie Dentaire, Dept. of Biology & Fundamental Materials, *Charles Livon Blvd., Jardin Emile Duclaux, 13007 Marseille, France*

Carried out in collaboration with the 'Institut de Medecine Dentaire' of Geneva (Switzerland), this project was intended for the study of the possibilities of remineralization of the demineralized dentinal zone existing at the front of the caries progression, when this zone is submitted to action from recalcifying solutions containing a heavy metal ion and fluor traces.

The calcic precipitates are examined on ground plano-parallel sections, with the aid of microradiography. Their composition will be determined with the aid of an electronic microprobe and X-ray diffraction.

The purpose of this study is to allow the development of dentine capping products which accelerate healing of the dentino pulpal wound.

SUPPORTED BY
Universite dAix Marseille funds n.a.

1.0191, TREATMENT OF CARIOUS LESIONS WITH POLYMERIC MATERIALS

C. Robinson, University of Leeds, School of Dentistry, Dept. of Oral Biology, *Blundell St., Leeds LS1 3EU, England, United Kingdom*

As a corollary to the department's interest in the chemistry of carious lesion development, interest has developed in the possibility of stopping or reducing the rate of enamel destruction during carious attack.

One area of current interest concerns the possible infiltration of material into the early developing lesion, attempting to occlude space and slow down or arrest the progress of attack.

A number of water-soluble polymers are under consideration, as substances capable of penetrating carious lesions and polymerize both in vivo and in vitro. Such materials slow down the progress of simulated carious attack in vitro.

SUPPORTED BY
University of Leeds funds n.a.

PREVENTION - DIET

1.0192, STUDY SENSORY PROPERTIES OF NEW DIHYDROCHALCONE ANALOGS

G. Crosby, Dynapol, *1454 Page Mill Rd., Palo Alto, California* 94304 (N01DE62479 (CONTRACT))

The objective of this research is to synthesize, physicochemically characterize, and evaluate the sensory properties and stability of new dihydrochalcone analogs in a search for a superior sweetener of commercial utility possessing, as nearly as possible, a taste quality comparable to that of sucrose. Evaluation of the properties of the new sweeteners shall include determination of purity, melting point, hygroscopicity, stability in the dry state, solubility in various solvents, sweetness ratings, and other sensory properties, and stability under a variety of conditions of manufacture, storage, and use.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0193, BIOCHEMICAL STUDIES ON A SWEETENER, SRI OXIME V

C. Mitoma, S R I International, *333 Ravenswood Ave., Menlo Park, California* 94025 (R01 DE 05466-01)

The objective of the proposed research is to conduct metabolic and pharmacokinetic studies on an artificial sweetener, SRI Oxime V. Absorption, distribution, and excretion of 14C-labeled Oxime V will be determined in rats and dogs. The pattern of formation of metabolites of Oxime V will be compared in mice, rats, dogs, and a subhuman primate. Isolated hepatocytes will be used to study the sequence of metabolite formation and to indicate any hepatoxic effects of Oxime V. A detailed pharmacokinetic study will be conducted in dogs. The biochemical and histopathologic effects on major internal organs will be studied in rats after they have been subchronically fed Oxime V.

Results from these studies will give the critical new information needed to further develop SRI Oxime V as an acceptable artificial sweetener.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $89,577

1.0194, CARIOGENICITY OF FOODSTUFFS

W.H. Bowen, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00240-02 CPR)

The public, dental profession and regulatory agencies have considerable interest in identifying those foodstuffs which have a high cariogenic potential. The purpose of this study is to develop a simple animal model which can be used to determine and to rank the cariogenic potential of common snack foods in a reproducible manner.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $22,694

1.0195, LONGITUDINAL CLINICAL STUDIES WITH SORBITOL CONTAINING SWEETS

J. Banoczy, Semmelweis Orvostudomanyi Egyetem, Conservative Dentistry Clinic, *Mikszath Kalman ter 5, 1088 Budapest V, Hungary* (1-19-0802-01-2/B)

The aim of the study is to determine the influence of sorbitol containing sweets given between meals on the caries increment of children aged 3-12 years in clinical longitudinal experiments. The experiment started with 535 children living in the closed community of the Children' City, Fot, Hungary. During three years the test group consumes daily sweets containing 8 gr. sorbitol, while the control group receives similar, but sucrose containing sweets. The evaluation is made yearly. The results of the first two years showed a considerable reduction in caries increment in the test group compared with the control group.

SUPPORTED BY

Scientific Research Council funds n.a.

PREVENTION - SALIVARY FACTORS

1.0196, INTERACTIONS OF SALIVA PROTEINS AND BACTERIA

S. Kashket, Forsyth Dental Center, Dept. of Chemistry, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 03430-06)

Much has been learned in recent years concerning the microbial and biochemical composition of plaque, and its importance in the etiology of dental caries is well documented. However, relatively little is known still about how plaque is formed. Two important aspects of plaque formation are the highly specific nature of bacterial colonization on the tooth surface, and the key role that certain salivary proteins play in interbacterial attachment, or aggregation, in the development of the enamel pellicle, and in the adhesion of specific bacteria to the surface of the tooth. Our objective is to study the basic molecular interactions that give rise to the adhesive phenomena and to apply these findings to the modification of plaque and the processes that contribute to its formation.

The proposal outlines studies for the isolation and characterization of the specific salivary aggregating factors and the surface receptors from strains of Streptococcus sanguis and S. mitis. The sanguis-specific factor has been purified with the use of sucrose density gradient centrifugation and isoelectric focusing and has been resolved into what appear to be non-identical macromolecular subunits. The receptor for the salivary factor has been solubilized from the cell wall of S. sanguis and is in the process of being further purified and studied. The isolated factor and receptor will be used in studies to determine the mechanisms that form the basis for bacterial adhesion and aggregation.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0197, EFFECTIVE IMMUNITY TO DENTAL CARIES - CELLULAR BASIS

J.R. McGhee, University of Alabama in Birmingham, School of Medicine, Dept. of Microbiology, *1919 7th Ave. S., Birmingham, Alabama* 35233 (R01 DE 04217-05)

The functional role of lymphoid cells, including the macrophages (M phi) and T and B lymphocytes and their soluble mediators in the induction of an IgA immune response will be studied in vitro. Optimal in vitro culture conditions for enumeration of IgA antibody (plaque) forming cells (PFC) following stimulation with T dependent antigens including DNP-Streptococcus mutans and TNP-erythrocytes, and lipopolysaccharide (LPS) as adjuvant from tissues including Peyer's patches (PP), mesenteric lymph nodes (MN), cervical lymph nodes (CN) and spleen (S) from CH3/HeN and C3H/HeJ mice will be evaluated. Single cell preparations or purified T and B cells from PP, MN, CN or S and M phi from spleen or peritoneum of E. coli K235 monoassociated mice will be immunized and incubated in Mishell-Dutton type cultures with LPS as adjuvant. The importance of monocyte (LAF monokine) and T cell (TRF) mediators and LPS on the induction of kinins, and their involvement in an IgA response will be established.

The origin of precursor IgA B cells and T cells in mucosal tissues including the saliva glands will be determined by examination of homing patterns of lymphocytes from gut-associate lymphoid-tissue (GALT) and MN, CN and other sources. Cell transfer experiments utilizing radioisotope methodology will be performed in groups of rats that are gnotobiotic, B cell suppressed, irradiated, or conventionalized in order to determine the origin of precursor lymphocytes. Furthermore, the efficacy of various modes of immunization in inducing antibodies in secretions will be assessed by tracing the homing patterns of antigen-sensitized cells to their sites of expression and by quantitating the immunological response utilizing fluorescent microscopy and serological techniques.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,

National Inst. of Health, National Inst. of Dental Research	$103,750

1.0198, DETERMINANTS OF FLUORIDE IN THE ORAL ENVIRONMENT

G.M. Whitford, Medical College of Georgia, School of Dentistry, Dept. of Oral Biology, *1459 Gwinnett St., Augusta, Georgia* 30902 (R01 DE 04832-02)

While it is widely accepted that fluoride exerts a cariostatic effect, the mechanism of this effect remains undefined. Further, it is unclear whether the fluoride in the oral fluids represents a significant source of fluoride for the enamel. Few of the variables which could conceivably influence the concentration of fluoride in the oral fluids have been studied and, indeed, the mechanisms of fluoride handling in certain of the oral fluids, namely the secretions of the minor salivary glands and the gingival fluid, have apparently received no study at all.

The proposed studies are designed to identify those variables which can influence the rates of fluoride delivery by the various oral fluids and the fluoride concentrations of these fluids. These fluids include mixed, whole saliva, the secretions of the parotid, submandibular, sublingual, and minor salivary glands, as well as the gingival fluid. The variables include flow rate, time of day, plasma fluoride concentration, the acid-base status of the systemic extracellular fluids and intraoral fluids, and the concentrations of Na ion, K ion, Cl-, Mg ions, Ca ions, PO4-3, CO2, H ions, and HCO3-. Several acute and chronic experimental approaches will be employed including the clearance and perfused duct techniques.

Results from these studies will provide a clearer understanding of the mechanisms of fluoride handling by salivary glands. Regional differences in the intraoral fluoride concentrations will be identified. In the long term, these results should contribute to an understanding of the cariostatic mechanism(s) of fluoride.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$36,566

1.0199, SALIVARY CALCIUM BINDING PROTEINS AND ORAL DISEASE

T.S. Freund, Fairleigh Dickinson University, Teaneck Hackensack Campus, School of Dentistry, Dept. of Biochemistry, *Teaneck, New Jersey* 07666 (R23 DE 05316-01)

Human salivary samples contain calcium binding proteins with binding constants of two categories: weak or strong binding. The proteins with weak binding constants are thought to be functionally involved with the reclacification process of enamel while the strong binding proteins may actually be involved with the regulation of the secretory process. It is proposed to isolate and characterize the calcium binding proteins with strong binding constants from human parotid saliva.

The calcium binding state in the human parotid and submandibular saliva may be a reflection of the clinical status. Patients with caries, cystic fibrosis and diabetes show abnormalities in their salivary calcium and in some cases, their calcium binding levels. This proposal is designed to study the relationship between the calcium binding proteins with strong constants and the clinical status of human salivary samples from heavy calculus formers, cystic fibrotics and diabetics over a three-year period.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$32,810

PREVENTION - COST/BENEFIT ANALYSIS

1.0200, COST EFFECTIVENESS OF VARIOUS CARIES PREVENTIVE AGENTS

N. Doherty, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Behavioral Sciences & Community Health, *Farmington Ave., Farmington, Connecticut* 06032 (N01DE52449 (CONTRACT))

Conduct a clinical field trial consisting of one control and seven treatment groups wherin the cost and clinical effectiveness of each of the following agents and procedures shall be assessed singly and in combination: Supervised topical fluoride applications; applications of bis-GMA pit and fissure sealants; and supervised mouthrinsing program with a fluoride solution.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$24,824

1.0201, COST ANALYSIS OF IMPLEMENTING SCHOOL-BASED COMMUNITY MOUTHRINSE PROGRAMS

J.A. Brunelle, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Biometry Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00225-03 CPR)

Data on costs of program, student participation and caries experience are being collected from seventeen communities throughout the U.S. and Guam which are conducting three-year demonstrations of school-based mouthrinse programs. Analysis of implementation, acceptance of community and cost-benefit will be performed during and after the three years.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $18,933

PREVENTION - CLINICAL TRIALS, GENERAL

1.0202, CONFERENCE ON ETHICS IN HUMAN DENTAL CARIES RESEARCH

J. Jenny, University of Iowa, School of Dentistry, Dept. of Dental Hygiene, *Jessup Hall, Iowa City, Iowa* 52240 (R13 DE 05192-01)

The objective of the proposed Conference is to interpret the principles and guidelines recommended by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research as they relate to dental caries research involving human subjects.

To accomplish these objectives the proposed conference will bring together persons of diverse backgrounds and interests from dental research and other disciplines. Presentations and discussions have been organized along the following lines. This first session will consist of expositories by two speakers on the ethical and legal aspects, respectively. Each subject will be amplified by discussants and by discussion from the floor. All sessions will be plenary. Sessions, II, III, and IV deal with the identification of ethical and legal problems in the conduct of three types of caries research involving human subjects: epidemiologic surveys, clinical trials, and behavioral or social research, respectively. A hypothetical research protocol specifying the research questions, study population, and procedures relating to each of these areas will be devised by members of the planning committee. The final session of the conference will provide an opportunity for summarizing the specific ethical and legal concern brought up in Sessions II, III and IV. In addition, concerns not raised in those sessions can be identified and discussed. Three primary speakers, representing the fields of epidemiology, clinical field research, and behavoral and social science, will summarize the specific ethical and legal consideration relative to their respective fields raised during Sessions II, III and IV. They will assess the impact of these considerations on their research domains. The final primary speaker will present an overview of the effects of these considerations on dental caries research, present and future.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0203, AN IMPROVED METHOD FOR ANALYZING CARIES CLINICAL TRIALS DATA

A. Kingman, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Biometry Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00223-03 CPR)

In many clinical trials the groups being compared at the end of the trial are not balanced as to initial DMFS scores, even though subjects were randomized to treatment groups initially. Two analytical methods have been used to adjust for these inbalances; the blocking analysis and the covariance analysis. The blocking analysis is the preferred method in that it requires fewer assumptions made of the data.

In this study an adaptation of Grainger's severity index, one method of summarizing the initial DMFS scores, was used as a blocking factor in the analysis of caries clinical trial data. This blocking factor has the advantage of being independent of the data set on which it is used. Further, its high correlation with initial DMFS scores insures that it is utilizing the existent information within subjects at the beginning of the trial. This analytical method was compared with other methods, including the covariance analysis and other blocking techniques to see what increase in efficiency would be realized by using this technique.

BIBLIOGRAPHIC REFERENCES: Kingman, A. A method of utilizing the subjects' initial caries experience to increase efficiency in caries clinical trials. Community Dentistry and Oral Epidemiology, 7:87-90, 1979.

SUPPORTED BY
U.S. Dept of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $2,887

PREVENTION - ANTIBACTERIAL

1.0204, PREVENTION OF DENTAL DISEASE IN NAVAL AND MARINE CORPS PERSONNEL BY INHIBITING PLAQUE ACCUMULATION

I.L. Shklair, U.S. Dept. of Defense, Navy, Naval Dental Research Inst., Microbiology Div., *Great Lakes, Illinois* 60088 (DN977592)

Dental and oral diseases are so universally prevalent and of such high levels in recruits that the total noneffective days are of staggering dimensions. The objective of this study is to prevent these plaque related diseases by inhibiting the buildup of plaque, by means of preventing the production of sticky substances (glucans) by oral bacteria.

Streptococcus mutans, the decay causing bacterium, produces an extracellular, water-insoluble sticky glucan that is related to the organisms' ability to cause decay. A variety of compounds will be tested for their ability to prevent the formation of insoluble glucans and to prevent plaques. Compounds, such as anionic and cationic detergents, lipids, and cations will initially be tested in vitro. Compounds that inhibit glucan formation will be tested in an animal caries-test model system. The materials that are non-toxic and demonstrate a high degree of caries inhibition in the animals will then be tested in human clinical trials.

SUPPORTED BY
U.S. Dept. of Defense, Navy,
Naval Medical Research &
Development Command,
National Naval Medical Center funds n.a.

1.0205, ANTIPLAQUES/FOOD ADDITIVES/OTHER AGENTS--ANTICARIES

S.L. Yankell, University of Pennsylvania, School of Dental Medicine, Dept. of Periodontics, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (N01DE52484 (CONTRACT))

Clinical testing of potential antiplaque and antimicrobial agents. Agents shall be applied both singly and in combination in vehicles such as mouthrinses and gels in various regimens and durations. Test groups shall not consist of more than 50 subjects. All testing shell be short term, i.e. 1-16 weeks. CORE MEASUREMENTS - plaques extent; dry weight, ph; microflora, gingivitis. ELECTIVE MEASUREMENTS - thickness; biochemistry; cervicular flow photography, pH.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $2,494

1.0206, CARIOGENIC STREPTOCOCCI TO PREVENT DENTAL CARIES

T. Shiota, University of Alabama in Birmingham, School of Dentistry, Dept. of Microbiology, *1919 7th Ave. S., Birmingham, Alabama* 35233 (N01DE62491 (CONTRACT))

The Contractor will select at least one strain from each of at least two different serotypes of S. mutans to conduct a research study on the use of mutants of cariogenic streptococci to prevent dental caries. These strains should produce abundant glucan and should be proven to be cariogenic in rodents.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $12,582

1.0207, USE OF MOUTHRINSE AS A DENTAL CARIES PREVENTION

S. Lotzkar, State University System of Florida, University of Florida, School of Dentistry, Dept. of Community Dentistry, *Gainesville, Florida* 32601 (N01DE72404 (CONTRACT))

Test the effectiveness in reducing new caries increment over a three year period of: a 0.5% sodium fluoride mouthrinse (0.0225% F) used daily in school; a 0.2% sodium fluoride (0.09% F) mouthrinse used daily in school; a 0.5% sodium fluoride mouthrinse used weekly in school; and a 0.2% sodium fluoride mouthrinse used weekly in school. To compare the effectiveness of the different concentrations and frequencies.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $81,833

1.0208, STRUCTURE AND MAINTENANCE OF EXTRACHROMOSOMAL DNA IN STREPTOCOCCI

D.B. Clewell, University of Michigan, Ann Arbor Campus, School of Dentistry, *Ann Arbor, Michigan* 48104 (P50 DE 02731-130019)

The objective of this work is to explore and characterize the nature of specific streptococcal plasmids and certain related plasmid-borne determinants. Attention will be given to several hemolysin-determining transmissible plasmids in S. faecalis. Emphasis will be on studies relating to the newly discovered sex hormone, or pheromone, in Streptococcus faecalis. This substance, which is produced by recipient strains, induces donors to become adherent, presumably to promote the cell-to-cell contact necessary for conjugation to occur. Attempts will be made to characterize the hormone, as well as the events involved in the induced mating response. Additional studies will explore whether other species of streptococci, especially members of the viridans group, excrete similar substances. These studies will include efforts to identify R-plasmids in members of the viridans group; and the question of whether members of this group can participate in gene transfer events will also be addressed. Other studies will concern the characterization of specific drug-resistance transposons (in S. faecalis) and certain interesting and unique behavior patterns of these elements. The effect of plasmids on the cariogenicity of certain cariogenic strains of S. faecalis will also be examined.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$271,583

1.0209, EFFECT OF CHEMOTHERAPY ON PLAQUE AND MICROBIAL ECOLOGY

W.J. Loesche, University of Michigan, Ann Arbor Campus, School of Dentistry, Dept. of Oral Biology, *Ann Arbor, Michigan* 48104 (R01 DE 03011-11)

Certain forms of human dental decay are associated with elevated levels or proportions of Streptococcus mutans. We are testing the hypothesis that S. mutans is reponsible for a measurable amount of this decay. One approach involve longitudinal studies in which the levels and proportions of S. mutans on caries-free fissures are being monitored at approximately 6-month intervals in order to determine whether S. mutans colonization and proliferation predisposes to caries in that fissure. In separate longitudinal studies, the acquisition of S. mutans by infants and the antraoral spread of S. mutans in adults is being investigated.

In a second clinical approach, rampant caries individuals, i.e., patients with more than or equal to 10 carious tooth surfaces, are being treated by private practitioners in their own offices using a protocol which includes short-term antimicrobial treatment in addition to the normal restorative procedures required by these patients. All patients receive the restorative treatment but only half receive the antimicrobial treatment and the other half receive a placebo treatment. Children 5 to 6 years of age, without any erupted permanent molars are treated either with 1.2% neutral NaF or a placebo gel. The gels are administered in applicator trays and are applied by the patients at home twice a day for a 1-week period at approximately six-month intervals. Fissure and proximal plaque samples and saliva are cultured before and after each gel treatment period for total viable counts, S. mutans and S. sanguis counts.

BIBLIOGRAPHIC REFERENCES: Svanberg, M.L. and Loesche, W.J. Implantation of Streptococcus mutans in man. Archs Oral Biol. 23, pp. 551-556, 1978. Svanberg, M.L. and Loesche, W.J. Intraoral spread of Streptococcus mutans in man. Archs. Oral Biol. 23, 557-561, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$110,064

1.0210, SPECIFIC DIETARY LIPIDS AS ANTICARIOGENIC AGENTS

J.J. Kabara, Michigan State University, School of Osteopathic Medicine, Dept. of Biomechanics, *Soil Science Bldg., East Lansing, Michigan* 48824 (R01 DE 04077-02)

Since it is generally accepted that microorganisms are the activating agents of dental caries and since dietary fats have been circumstantially implicated as having some anticariogenic effects, our proposed research will investigate the role of antimicrobial lipids as potential anticariogenic agents. Our past research has explored basic relationships between lipid structure and their antimicrobial activity. Based on this background, we will elucidate similar structure-function in vitro relationships between lipids and Streptococcus mutans. We will then compare in vitro antimicrobial activity of specific lipids with their effects on the development of dental caries in the several rat model systems. Caries scoring done at Michigan State University for all experimental groups will be periodically checked by other investigators in a double-blind evaluation. Both the kind and levels of antimicrobial lipids in the diet necessary to prevent animal caries will be determined.

BIBLIOGRAPHIC REFERENCES: Antimicrobial Lipids: Natural and Synthetic Fatty Acids and

Monoglycerides. J.J. Kabara, R. Vrable and M.S.F. Lie Ken Jie, Lipids 12:753-759 (1977). Prevalence of Dental Caries and S. mutans CFU in Rats Fed NIH diet 2000 modified with Antimicrobial Lipids. C.J. Pressler, Rachel Schemmel and J.J. Kabara, FASEB, 36:1133, 1977.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0211, STUDY OF THE ANTIMICROBIAL EFFECTS OF FLUORIDE

L.R. Brown, University of Texas, Health Science Center at Houston, Dental Branch, Dept. of Pathology, *6515 Freeman, Houston, Texas* 77025 (R01 DE 04542-03)

The study aim is to determine the effects of fluoride on the growth and metabolism of cariogenic Streptococcus mutans. The goals of the current year were to screen five potential mechanisms of sodium fluoride inhibition in strains differing in fluoride sensitivity: 1) growth; 2) viability; 3) metabolism; 4) adherence; and, 5) fluoride adaptation/mutation.

The bacteriocidal action of fluoride (600 ppm) for fluoride-sensitive and fluoride-resistant strains was temperature and pH dependent. The antimetabolic actions of fluoride were assessed by: 1) carbohydrate fermentation patterns; 2) substrate utilization and endproduct synthesis; 3) intracellular polysaccharides (IPS) and enzyme production; and, 4) glucose uptake. Fluoride effects on adherence were studied by comparing gross plaque accumulation on extracted teeth exposed to 5% sucrose fluoride-free cultures of fluoride-sensitive and fluoride-resistant strains. Fluoride therapy can generate S. mutans strains that adapt to fluoride and demonstrate a phenotypic expression of fluoride resistance that is rapidly lost in the absence of fluoride.

The present findings indicate that fluoride may affect S. mutans in ways dependent on fluoride concentration, age of cell, natural or induced fluoride sensitive and nature of the environment.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0212, POTENTIAL ANTICARIES AGENTS

R.J. Doyle, University of Louisville, School of Medicine, Dept. of Microbiology & Immunology, *101 W. Chestnut, Louisville, Kentucky* 40202 (R01 DE 05102-02)

The widespread use of sucrose as a dietary constituent has resulted in the magnification of dental caries. Periodically, local and national programs are developed which are designed to curb the sucrose-delay syndrome. Currently, dental caries can be partially controlled by fluoridation of water supplies, antibiotics, certain types of immunological reactions, or the use of dextranase, a glucan-degrading enzyme. Only fluoridation has been effective for controlling caries in terms of mass populations. In the proposed research, we plan to synthesize new derivatives of sucrose which may have potential benefit in reducing the incidence of caries. The plan is to develop site-directed irreversible enzyme inhibitors (affinity labels) for Streptococcus mutans glucosyltransferases, key bacterial enzymes implicated in the initiation and maintenance of carious lesions. The affinity labels will consist of sucrose molecules to which have been added chemically reactive groups that can irreversibly inactivate sucrose-binding enzymes. This research is a new and alternate approach to the prevention of caries. The affinity labels will be synthesized, characterized and tested for their capacity to selectively inactivate S. mutans glucoslytransferases. Additional experiments will evaluate the effectiveness of the affinity labels to inhibit insoluble and soluble glucan synthesis and to inhibit the adherence of S. mutants to smooth surfaces. Ideally, properly designed and effective affinity labels could be added to foods, beverages, etc., and result in the enhancement of oral health. These studies may reveal new and important leads to combatting dental caries, and concomitantly enhance the public's willingness to use sucrose with confidence.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $56,861

1.0213, BACTERIOCINS AS POTENTIAL CARIES CONTROL AGENTS

R.E. Morhart, University of Miami, School of Medicine, Dept. of Microbiology, *1400 N.W. 10th Ave., Box 520875, Coral Gables, Florida* 33152 (R23 DE 04165-03)

Dental caries is essentially a microbial disease of childhood and is a major health problem in our society. Considering the bacterial nature of dental plaque and the current knowledge of the role of Streptococcus mutans in the etiology of dental caries, it is logical to predict that of all the approaches to the control of caries the antimicrobial route, especially the use of antibiotics, could be one of the most effective. This proposal is concerned with an in-depth study of the potential usefulness of highly specific antimicrobial agents, the bacteriocins, for the control of dental caries. In the first phase of this study we have identified a number of microorganisms which produce bacteriocins active against all serotypes of S. mutans. We have also isolated and partially purified two of these bacteriocins. In later studies these purified bacteriocins are to be tested in animal models to determine their ability to inhibit caries induction by eliminating the microorganisms which are etiological agents. This approach is based on the expectation that these bacteriocins will eradicate the causative organisms when applied locally in the oral cavity, like antibiotics.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0214, PRECLINICAL SCREENING OF ANTICARIES AGENTS

R.J. Shern, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Preventive Methods Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00112-06 CPR)

The objective of this project is to identify anticaries agents suitable for short-term clinical trials. Screening is conducted both in vitro and in animals. The in vitro studies measure minimal inhibitory concentration, and modification of enamel dissolution rate. Other measurements are used electively depending on the nature of the agent. The animal studies measure the effects of an agent on dental caries and plaque. Several bisguanides screened favorably providing marked inhibition of dental caries and plaque. A solution that changes some surface enamel to CaHPO42H2O (dical) promoted uptake of fluoride by the enamel with no change in its surface morphology. The effects of the dical forming solution on dental caries are being studied.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $28,768

1.0215, SHORT-TERM CLINICAL TRIALS OF ANTI-PLAQUE AGENTS

R.J. Shern, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Preventive Methods Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00113-06 CPR)

The objectives of this project are: (1) to identify, adapt and pretest methods of measuring dental plaque and its bacterial and chemical composition; (2) to conduct short-term clinical studies of agents which might be capable of restricting plaque caries. These studies will measure the safety and presumptive efficacy of anti-plaque agents.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $13,374

1.0216, ANTIMICROBIAL SUSCEPTIBILITY OF STREPTOCOCCUS MUTANS

W.A. Little, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00185-04 CPR)

The antibiotic susceptibility of strep. mutans has been examined. From the results of screening experiments with Oxoid multidiscs, twelve antibiotics were selected for MIC determinations using a broth microtiter technique.

BIBLIOGRAPHIC REFERENCES: Little, W.A., Thomson, L.A. and Bowen, W.H.: Antibiotic Susceptibility of Streptococcus mutans: Comparison of Serotype Profiles. Antimicrobial Agents and Chemotherapy, 15:440-443, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $28,994

1.0217, EFFECT OF INTERACTION BETWEEN AMINE DERIVATIVES AND CHLORHEXIDINE ON RAT CARIES

C. Emilson, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of

Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00271-01 CPR)

The present study was designed to compare the effect on caries activity in rats by topical application of chlorhexidine with different concentrations and frequencies with and without the addition of the basic amino acid lysine. Plaque score, the proportion of S. mutans of total count in plaque and caries decreased with increasing concentration and frequency of chlorhexidine application. The addition of lysine did not enhance the effect.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$19,959

1.0218, EFFECT OF TOPICAL APPLICATIONS OF ANTIMICROBIAL AGENTS ON THE PLAQUE FLORA IN PRIMATES

C. Emilson, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00272-01 CPR)

Four unknown compounds supplied by manufacturers were tested in primates in the search for promising antimicrobial agents to prevent dental plaque formation and caries activity. Changes in the population of dental plaque organisms were examined by using Fluorescent Antibody (FA) reagents specific for S. mutans, S. sanguis and four species of Actinomyces. An increase in the proportion of S. sanquis and a reduction of Actinomyces was observed with decreasing plaque scores. For two of the agents this effect was equal to or more pronounced than that obtained with chlorhexidine which served as a control.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$13,710

1.0219, THE EFFECT OF MOUTHWASH - CP-101 - ON DENTAL PLAQUE AND GINGIVITIS

J.H. Miyares, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Section, *Bay Pines, Florida* 33504 (516-002-F)

This investigation was initiated to determine the clinical efficacy of Mouthwash CP-101. Two hundred subjects were screened and gingivitis and plaque intensity scores were recorded and subjects photographed.

Subjects used 16 ml of mouth rinse, experimented or control, twice daily for a period of six months. Gingivitis severity and plaque intensity scores were recorded at 30, 60 and 180 days following initiation of mouthwash use and the subjects were photographed.

Evaluation of the data revealed clinical significant reduction on the gingivitis severity and plaque intensity scores. It was also noticed that the continued use of CP-101 mouthwash left a dark brownish stain on the surface of the enamel in a high percentage of the subjects.

Routine prophylaxis procedures were not sufficient to eliminate the stain because of its tenacity.

It has been concluded that in spite of the promising clinical significance of CP-101, the secondary effect of staining anterior teeth renders the mouthwash cosmetically unacceptable. Additional studies should be carried out with similar mouthwashes that might not have the negative side effects.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

1.0220, POSSIBLE USE OF MEDIUM CHAIN FATTY ACIDS TO PREVENT DENTAL CARIES

M.L. Hayes, University of Bristol, Dept. of Biochemistry, *Bristol BS8 1TH, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$9,566

PREVENTION - ANTIPLAQUE

1.0221, THE EFFECT OF FLUORIDE MOUTHRINSES ON BACTERIAL PLAQUE ACCUMULATION

N. Tinanoff, University of Connecticut, Health Center, School of Medicine, *Farmington Ave., Farmington, Connecticut* 06032 (DAMD17 77 C 7058)

Identify topical fluorides which alter bacterial adsorption to enamel and to clinically test these agents to develop a safe and effective regimen to reduce dental plaque accumulation, and thereby, dental disease.

In the first phase, interference with bacterial adsorption to enamel due to fluorides will be investigated in vitro by placing enamel cylinders in bacteriological broth to two oral isolates, s. Mutans and s. Sanguis, while exposing the cylinders to four different fluorides twice a day. The number of bacteria attached to enamel will be used as model to determine the type of fluoride that will best alter bacterial sorption to enamel. In the second phase, a double blind clinical trial of cross-over-design entailing 40 young adult subjects will be performed using the most effective regimen found from the previous experiments.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research	$40,276

1.0222, DEVELOPMENT OF THERAPEUTIC METHODS TO PREVENT ORAL DISEASES OF NAVAL AND MARINE CORPS PERSONNEL

L.G. Simonson, U.S. Dept. of Defense, Navy, Naval Dental Research Inst., Microbiology Div., *Great Lakes, Illinois* 60088 (DN977619)

Dental plaque control is part of a Navy-wide preventive effort to improve oral health of Naval personnel. The accumulation of dental plaque on teeth depends largely on adhesive metabolic products of certain oral organisms. The objective of this study is to evaluate enzymatic methods to degrade these adhesive components, thereby identifying potential therapeutic agents to reduce or eliminate dental plaque on the teeth of Naval personnel.

A new enzyme which hydrolyzes water-insoluble glucans (alpha 1,3-glucanase) will be produced and evaluated for its efficacy in preventing oral disease in rodents. Dextranase modification to achieve a preparation which has a greatly increased affinity for dental enamel surfaces while maintaining its hydrolytic function will also be used on selected Navy volunteers. Other means of interfering with adherence and some of the actual mechanisms of bacterial binding to oral surfaces will be studied.

SUPPORTED BY

U.S. Dept. of Defense, Navy, Naval Medical Research & Development Command, National Naval Medical Center	funds n.a.

1.0223, ENZYMATIC PREVENTION OF DENTAL PLAQUE FORMATION

D.L. Williams, Abcor Inc., *850 Main St., Wilmington, Massachusetts* 01887 (N01DE62493 (CONTRACT))

A study designed to develop an enzyme mixture which effectively and safely prevents plaque accumulation and dental caries. Conduct a biphasic screening program involving a preliminary in vitro evaluation on human dental plaque followed by testing in the rat and leading to the formulation of an enzyme mixture which effectively and safely prevents plaque and dental caries. The first phase will specifically involve the systematic determination of the composition of the enzyme mixture which is most effective in vitro in dispersing and/or solubilizing: freshly collected human dental pellicle and supragingival plaque; and plaque formed on human tooth crowns incubated in vitro in a growth medium consisting of freshly collected human saliva innoculated with Strep. mutans. Determination of the in vivo antiplaque and anticaries effectiveness of the enzyme mixture will be conducted at Tufts University, using the National Caries Program's standard Norway rat screening procedure.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0224, A COLLABORATIVE STUDY OF THE EFFECTIVENESS OF PLAQUE CONTROL PROGRAM FOR THE PREVENTION OF DENTAL DISEASES IN DIFFERENT VA PATIENT POPULATIONS

C.J. Toga, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *200 Springs Rd., Bedford, Massachusetts* 01867 (581-001-P)

PURPOSE: To determine the effectiveness of a standard dental plaque control instructional program in different VA patient populations.

METHOD: Initial random selection of 30 patients with at least 16 natural teeth. Initial examination included intra-oral radiographs and kodachrome slides. Patients were re-examined at 6 months, 12 months and 24 months. A trained instructor (not examiner) taught plaque control to patients. Final sample size is 16 and data collection is complete. Data is being prepared for processing.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

1.0225, THE PREVENTION OF DENTAL DISEASE IN CHILDREN BY FREQUENT PROPHYLAXES

R. Duckworth, University of London, London Hospital Medical College, Dept. of Oral Medicine & Periodontology, *Turner St., London E1 2AD, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$25,367

PREVENTION - ENAMEL SEALANTS & SURFACE MODIFIERS

1.0226, FEASIBILITY STUDY ON A PROCESS FOR ELECTROLESS METAL DEPOSITION IN PITS AND FISSURES OF TEETH FOR USE IN PREVENTIVE DENTISTRY

T.J. O'Keefe, University of Missouri, Rolla Campus, School of Engineering, Dept. of Metallurgical & Nuclear Engineering, *Rolla, Missouri* 65401 (DADA17-73-C-3087)

To study applicability of unique techniques and processes for applying metalpolymer combinations to pits and fissures of teeth to positively prevent these surfaces from attack by decay. Present military preventive dentistry techniques are time consuming, require multiple visits, and provide a reduction in caries incidence and still require patient home care. In the military it is impossible to treat all present caries and fluoride applications must be applied yearly, or every six months in many cases, requiring an extensive time consuming preventive dentistry effort. Success in this effort will mean a one time treatment for all personnel that will positively prevent the development of new carious lesions.

Procedures will be developed to apply various combinations of electroless metal-polymer films to the pit and fissure area of teeth. briefly, this consists of chemical sensitization and activation of a tooth to allow electroless supposition, by electron transfer, of thin metal films over the desired area of the tooth. The goal is to provide true chemical bone and/or minimally a vastly improved mechancal bond. The technique is similar in nature to those presently used for producing a metallic coating on a nonconductive substrate, e.g, plastic or ceramic material.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research	$45,160

1.0227, NAVY ENVIRONMENT - CONTROL OF DENTAL CARIES IN NAVY PERSONNEL

H.W. Lyon, American Dental Assn., Health Foundation, *211 E. Chicago Ave., Chicago, Illinois* 60611 (N00014-78-C-0179)

This investigation is intended to determine the biochemical basis for improving the efficacy of preventive dental treatment procedures on oral tissues in Naval personnel. It is being carried out in collaboration with the Naval Dental Research Institute, Great Lakes, Illinois.

Electron probe analysis and electron microscopic steroscanning techniques will be used to evaluate the effects of polyvalent cations alone and in combination with fluoride on the demineralization and remineralization of tooth enamel. In addition, through the use of standard animal model, the effectiveness of various delivery modes of fluoride in combination with polyvalent cations will be evaluated.

SUPPORTED BY

U.S. Dept. of Defense, Navy, Office of Naval Research	$25,005

1.0228, EFFECTS OF VARNISH AND TRACE ELEMENTS ON ENAMEL FLUORIDE AND DENTAL CARIES

D.H. Retief, University of Alabama in Birmingham, School of Dentistry, Dept. of Biomaterials, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130036)

One of the objectives is to evaluate in vitro and in vivo fluoride uptake by enamel from topical fluoride varnishes. Calcium fluoride is the main reaction product when topical fluoride agents are applied to enamel surfaces. Fluoride-containing varnishes have been introduced to prolong the contact time of topically applied fluoride to enamel and thus promote the formation of fluoroapatite.

The application of fluoride-containing varnishes to enamel resulted in significantly increased fluoride uptake, distribution and retention when compared to acidulated phosphate fluoride. An interesting finding in this in vitro study was that the fluoride uptake by enamel was inversely related to the fluoride concentration of the enamel prior to topical fluoride application.

The relationship between enamel fluoride content and caries experience in a community living in an endemic fluoride area with fluoride content in the drinking water of 3.2 ppm was determined. A highly significant positive association between caries experience and enamel fluoride concentration was established.

It is proposed to further investigate the acquisition of fluoride by enamel after treatment with fluoride-containing varnishes. Particular attention will be paid to the retention of the acquired fluoride after prolonged immersion in synthetic saliva and the effect of more frequent topical applications on fluoride uptake.

The caries inhibitory effect of the fluoride-containing varnishes will be evaluated in the rat, and attempts will be made to relate caries inhibition with enamel fluoride concentration.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $60,014

1.0229, EFFECT OF FISSURE SEALANT ON PROGRESS OF DENTAL CARIES

S.L. Handelman, Eastman Dental Center, Dept. of General Dentistry, *800 Main St. E., Rochester, New York* 14603 (R01 DE 03713-04A1)

The objective of this study is to a) evaluate the effect on initiation and progression of dental caries when carious and non-carious occlusal pits and fissures are sealed with an ultraviolet light polymerized sealant, Nuvaseal, for time period up to five years, b) compare the costs and benefits of that procedure to the use of conventional restorative techniques, and, c) compare the efficacy of an ultraviolet light polymerized sealant, Nuvaseal, with an autopolymerized sealant, Delton, in regard to objectives (a) and (b).

Children from 5-15 years of age will have all previously untreated non-carious and carious (no greater than one half dentin penetration) occlusal surfaces of permanent posterior teeth sealed with either Nuvaseal or Delton. A third treatment regimen will restore only carious occlusal surfaces with amalgam. Permanent occlusal surfaces with deeper caries penetration and all other surfaces of permanent and deciduous teeth will be restored with conventional filling materials when indicated.

The initiation of new carious lesions and the progress of existing lesions will be evaluated clinically and radiographically. The costs and the benefits of sealants and traditional restorative procedures will be compared over a period of time that would enable the determination of the impact of proximal caries. Nuvaseal and Delton will be compared with regard to retention rate, effect on initiation and progress of caries, and comparative time and ease of application.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $96,009

1.0230, F-RELEASING AND ACID BARRIER-POLYMER CARIES THERAPIES

H.R. Rawls, Louisiana State University, Medical Center, School of Dentistry, Dept. of Biomaterials, *1542 Tulane Ave., New Orleans, Louisiana* 70112 (R01 DE 04749-03)

The objective of this project is to explore and develop new means of controlling caries by investigating methods of interfering with the transport of mineral out of tooth structure. Polymer or polymer-forming formulations are to be deposited inside early, subsurface, lesions. The polymer systems to be investigated are those which can be expected to operate as diffusion barriers and/or by releasing fluoride into the local lesion environment.

Several polymer systems have been studied: phenol/aldehydes, the fluoride salts of amine-substituted monomers, phosphonate-substituted monomers, hydroxyl-substituted monomers, and preformed polymers with phosphonate and/or fluoride-releasing pendant groups.

The fluoride salts of several amine-substituted monomers were found to be capable of rapid homo- and copolymerization at mouth temperature in bulk, and in aqueous and alcoholic solutions. The most promising of these materials fully permeates subsurface enamel lesions when applied with a brush, and polymerizes in 10-15 min as a highly crosslinked terpolymer. Untreated lesions were found to release 3 times the amount of phosphate in weak acid buffer as did lesions treated with the terpolymer. It releases a total of 8 mg fluoride/g at a decreasing rate over four days in neutral buffer, during which time it adsorbs only 4 percent by weight of water.

A preformed polymer containing phosphonate pendant groups was found to have a strong adsorption affinity for hydroxyapatite. This polymer forms a protective film when applied from 50 percent ethanol. A monomolecular layer provides substantial protection against weak acid demineralization. Such a material could serve as a protective mouthrinse.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $10,583

1.0231, POLYMERIC POLYPHOSPHONATES ON DENTAL CARIES AND PLAQUE

M. Anbar, State University of New York, Health Science Center at Buffalo, School of Medicine, Dept. of Biophysical Sciences, *3435 Main St., Buffalo, New York* 14214 (R01 DE 05327-01)

Polymeric polyphosphonate will be applied in dental research to meet different goals. These include caries prevention, dental plaque inhibition and elucidating the mechanism of cariogenesis and of the mode of action of different cariostatic agents including fluorides. The effect of polymeric polyphosphonates and the mode of action will be compared with those of nonomeric polyphosphonates e.g. diphosphonates.

The polymers to be synthesized and studied include hydrophilic and hydrophobic polymeric polyphosphonates, polyphosphonates carrying carboxylic, and quarternary ammonium groups as well as polymeric polyphosphonates which carry copolymeric groups which slowly release fluoride ions as well as different bacteriocidic phenols. The Ca ions and F activities in plaque will be determined in vivo and in vitro at different levels of polymeric polyphosphonate treatment as funtion of time. The caries inhibition will be studied in vivo on rats infected with Streptococcus mutans while the plaque inhibition studies will be carried out in vitro on tooth slabs in the presence of the same bacteria.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$116,040

1.0232, TASTE AND ITS DISORDERS

R.O. Wolf, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Oral & Pharyngeal Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00212-03 CI)

For summary: see 4.0072.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$17,301

1.0233, DEVELOP METHOD OF INTRAORAL TELEMETRY OF VARIOUS IONS

R.J. Shern, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Preventive Methods Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00234-02 CPR)

Oral biotelemetry is being developed which enables direct and continuous measurements of intraoral responses such as H plus and F minus levels following ingestion of various foods and therapeutics. Measurements of ionic levels may be conveyed to the recording equipment by radio or wire transmission. Clinical studies will be initiated soon.

Data from telemetry coordinated with data from other projects will aid in the evaluation of various food stuffs for their relative cariogenicity.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$15,486

1.0234, COMPARISON OF THE RETENTION OF TWO BIS-GMA PIT AND FISSURE SEALANTS

S. Li, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Biometry Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00266-01 CPR)

The retention of bis-GMA pit and fissure sealants polymerized chemically (Delton) or by ultraviolet light (Nuva-Seal) is being compared. Different analytic methods for categorical data will be used to determine the effect of different treatments, tooth types and length of time on percent retention.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$14,887

1.0235, SEALANT EFFECTS ON CARIES-LIKE ENAMEL LESIONS IN VITRO

M.J. Hicks, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Hwy. 6 W., Iowa City, Iowa* 52240 (584-001-P)

Artificial caries-like lesions will be produced on freshly extracted canines, premolars and molar teeth. The artificial caries medium utilizes a 15 percent acidified gelatin gel. The specimens are painted with an acid-resistant varnish with the exception of 1 mm by 4 mm enamel windows which remain exposed to the artificial caries medium.

Once the artificial caries-like lesion has developed sufficiently, the teeth will be slit in half. In the acid-etch portion of the study, the teeth halves will be treated with varying phosphoric acid concentrations, varying time exposures to the acid, and fluoride treatment prior to or following acid-etching with acidulated phosphate fluoride, sodium fluoride or stannous fluoride. One group will be acid-etched only with no fluoride treatment.

In the resin penetration portion of the study, each tooth half will be labelled such that it receives the same acid concentration, exposure time and fluoride treatment as the half from the same tooth in the first part of the experiment. These halves will then be sealed with an ultra-violet polymerized sealant or a chemically polymerized sealant. Caries-free specimens will also be sealed for comparison.

The effects of various phosphoric acid concentrations, exposure times and resin penetration will be examined and comparisons made. The histologic methods involved will be scanning electron, polarized light, transmitted light and ultraviolet light microscopy. The results will enable the investigator to determine the optimal phosphoric acid concentration, time exposure and fluoride agent to produce cariostasis in enamel caries-like lesions.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

1.0236, INVESTIGATIONS ABOUT THE ADHESION AND THE PENETRATION-DEPTH OF ACID-ETCH-FILLING MATERIALS AND THEIR BACTERIOLOGICAL COLONIZATION

H. Tschamer, Universitat Klinik fur Zahn Mund und Kieferheilkunde, Dept. of Preventive Dentistry, *A8036 Graz, Austria*

The investigation deals with clinical light and REM studies about the adhesion and penetration depth of composite materials in the Acid-Etch-technique.

Methods for a better adhesion without enamel-irritation should be developed. At the same time differences in the bacteriological colonization on SAT-restorations and the healthy enamel and their effects should be investigated.

SUPPORTED BY

Osterreichischer Fonds zur Forderung wissenschaft. Forschung	funds n.a.

1.0237, PENETRATION OF TOOTH TISSUES BY THE DIFFERENT FILLING MATERIALS

C. Hurel, Universite dAix Marseille, Faculte de Chirurgie Dentaire, Dept. of Pedodontics, *Charles Livon Blvd., Jardin Emile Duclaux, 13007 Marseille, France*

This projects is, at the moment, undertaken by the Pedodontics Department:

Study of a new pits and fissures sealant on behalf of the French Laboratory Pierre Rolland.

The idea is to fill the pits and fissures of teeth that are to be extracted for orthopedic purposes, and after cutting them, study the degree of penetration under the electronic microscope.

With the same technic as above, the study of the penetration of tooth tissues, on deciduous teeth, by the different filling materials used in pedodontics will be performed.

SUPPORTED BY

Universite dAix Marseille	funds n.a.

PREVENTION - FLUORIDE, TOPICAL

1.0238, THE EFFECT OF A LOW FLUORIDE DELIVERY SYSTEM ON BACTERIAL METABOLISM

N. Tinanoff, University of Connecticut, Health Center, School of Medicine, Dept. of Biomedical Sciences, *Farmington Ave., Farmington, Connecticut* 06032 (DAMD17 78 C8066)

A. To study the effect of various fluoride compounds at low concentrations on the the metabolism of known disease producing oral bacteria. B. To determine the practicality and effectiveness of a slow release fluoride system in altering plaque formation, thus preventing/reducing incidence of acute and chronic gingivitis.

For the in vitro portion of the project, enamel cylinders will be prepared from extracted bovine molars. The cylinders will then be placed in test tubes containing media inoculated with proper organisms and containing the appropriate flouride agent and concentration under study. if bacterial growth inhibition is apparent for any of tested compounds, procedure will be repeated at lower concentrations with the agent noted to affect growth. The in vivo phase of the study will involve hamsters receiving intermediate restorative material restorations with and without fluoride for slow release. At completion of appropriate time interval, specified molars will be extracted and analyzed for fluoride effects.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Medical Bioengineering Research & Development Lab.	$493

1.0239, EVALUATION OF ANTIMICROBIAL AGENTS ON DISEASE PRODUCING ORGANISMS OF THE ORAL CAVITY OF NAVAL RECRUITS

I.L. Shklair, U.S. Dept. of Defense, Navy, Naval Dental Research Inst., *Great Lakes, Illinois* 60088 (DN541302)

The objective of this study is to test various therapeutic agents against oral disease producing bacteria. The bacterium, streptococcus mutans, is the prime etiologic agent of dental decay; the elimination of this organism would dramatically improve the oral health and combat readiness of Navy and Marine Corps personnel. Various agents will be tested to determine if the compounds will (1) eradicate this organism from the mouth, (2) reduce the numbers of infected sites on the teeth, and/or (3) reduce the number of organisms at the infected site.

Antimicrobial agents will be applied on floss or on an absorbent yarn and passed through the space between the teeth - an area where strep. mutans preferentially colonizes. Initially a 10% stannous fluoride solution will be applied using floss, and the effect on the numbers and distribution of strep. mutans on the teeth will be determined before and after treatment. This is a new technique in a clinical trial for plaque control in a preventive dentistry program.

SUPPORTED BY

U.S. Dept. of Defense, Navy, Naval Medical Research & Development Command, National Naval Medical Center	funds n.a.

1.0240, FLUORIDE ADMINISTRATION IN CONTROLLING DENTAL CARIES

K.H. Lu, Oregon State Higher Education System, University of Oregon Health Sciences Center, School of Dentistry, Dept. of Pedodontics, *611 S.W. Campus Dr., Portland, Oregon* 97201 (N01DE42444 (CONTRACT))

OBJECTIVES AND WORK SCOPE: This is a clinical trial designed to determine whether high-level, short-term application of fluoride is more efficacious than a low-level, long-term method. A comparison will be made between five-minute applications of acidulated phosphate fluoride gel (1.23% F) in custom-fitted trays for 10 consecutive school days under dental hygienists' supervision and a one-minute use of fluoride mouthrinse (0.023% F) each school day for the duration of two school years. The comparative effectiveness of these two modes of application would be determined by the dental caries experience of study subjects.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0241, FLUORIDE RELEASING SYSTEM FOR ORAL USE

D.R. Cowsar, Southern Research Inst., *2000 9th Ave. S., Birmingham, Alabama* 35205 (N01DE42446 (CONTRACT))

The objective of this research project is to develop a fluoride-containing material that: will release fluoride at a constant predetermined linear rate for a period of at least six months without maintenence or adjustment; can be easily applied or attached in the mouth (attachment to a tooth or teeth by adhesive or orthodontic bands, or as part of a spacemaintainer, or a simple adhesive coating); can be completely and safely removed at any time; and should contain materials that exhibit a very low order of toxicity in animals, are harmless to the teeth and harmless to and non-absorbable through the oral and gastrointestinal mucoas.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$15,094

1.0242, EVALUATE ORAL RINSING WITH A SODIUM MONOFLUOROPHOSPHATE

L.A. Friedman, University of Texas, Health Science Center at Houston, Dental Branch, Dept. of Preventive Dentistry, *6515 Freeman, Houston, Texas* 77025 (N01DE62496 (CONTRACT))

The Contractor proposed to design and implement a three-year longitudinal clinical trial to study the effect of supervised oral rinsing with a sodium monofluorophosate mouthrinse on preventing dental caries in children. A population of approximately 900 subjects from an area that has low fluoride in its drinking water will be utilized.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0243, EFFECT OF TOOTH-CLEANING ON SODIUM FLUORIDE RINSE

D.H. Leverett, Eastman Dental Center, *800 Main St. E., Rochester, New York* 14603 (N01DE72407 (CONTRACT))

This project is for a longitudinal clincial research study in which the effect upon dental caries of weekly mouthrinsing with a 0.2% sodium fluoride solution without prior cleaning of the teeth will be compared with the effect of rinsing preceded by cleaning of the teeth, either with a toothbrush alone or with a toothbrush and dental floss.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$54,098

1.0244, COMPARISON OF FLUORIDES IN CARIES PREVENTION

D.E. Skinner, Applied Management Sciences Inc., *962 Wayne Ave., Suite 701, Silver Spring, Maryland* 20910 (N01DE72411 (CONTRACT))

This project is for a longitudinal clinical trial to determine the effect on dental caries of neutral sodium fluoride (NaF) and acidulated phosphate-fluoride (APF) when each is used as a tablet and as a solution. The study population will comprise approximately 1,625 school children, 12-14 years old, who reside in a community where the drinking water contains less than 0.3 ppm fluoride and the school population is relatively stable.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$106,075

1.0245, EFFECT OF MOUTHRINSING WITH FLUORIDES

L.A. Friedman, University of Texas, Health Science Center at Houston, School of Public Health, Dept. of Human Ecology, *6515 Freeman, Houston, Texas* 77025 (N01DE82416 (CONTRACT))

The Contractor will implement a 3-year longitudinal clinical trial to study the effects of mouthrinsing with stannous fluoride and sodium fluoride upon the development of dental caries, dental plaque, gingivitis, and extrinsic tooth staining. A test population of approximately 500 students will be utilized, one half of the subjects rinsing once a day in school with 10 ml. of a 0.1% solution of stannous fluoride (SnF-2) and the other half rinsing once a day in school with 10 ml. of a 0.05% solution of sodium fluoride (NaF).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0246, EFFECT OF DAILY MOUTHRINSING WITH FLUORIDES

D.H. Leverett, Eastman Dental Center, *800 Main St. E., Rochester, New York* 14603 (N01DE82417 (CONTRACT))

The Contractor will implement a 3-year longitudinal clinical trial to study the effects of mouthrinsing with stannous fluoride and sodium fluoride upon the development of dental caries, dental plaque, gingivitis, and extrinsic tooth staining. A test population of approximately 500 students will be utilized, one half of the subjects rinsing once a day in school with 10 ml. of a 0.1% solution of stannous fluoride (SnF-2) and the other half rinsing once a day in school with 10ml. of a 0,05% solution of sodium fluoride (NaF).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0247, EFFICACY OF PRIOR TOOTHCLEANING ON FLUORIDE TREATMENT

L.W. Ripa, State University of New York, Health Science Center at Stony Brook, School of Dentistry, Dept. of Childrens Dentistry, *Stony Brook, New York* 11790 (N01DE92419 (CONTRACT))

This procurement is for the conduct of a longitudinal study to assess the effect of prior toothcleaning upon the anti-caries efficacy of semi-annual professionally applied topical fluoride treatments. The proposed study will provide a comparison of the efficacy of semi-annual professionally administered APF gel treatments when preceded by either conventional pumic prophylaxis, self-cleaning of the teeth by subjects using a toothbrush and dental floss, or no tooth cleaning.

Three study groups will be established, each containing approximately one-third of the subjects at the beginning of the study. Subjects will be randomly assigned to groups. Subjects in Group I will receive semi-annually a professional application of acidulated phosphate fluoride gel that contains 1.23% fluoride and has a pH of approximately 3.0. Each gel application will be preceded by a thorough dental prophylaxis. Calculus will be removed as necessary. Group II will receive semi-annual fluoride gel applications, clean their own teeth with a toothbrush, dentifrice, and dental floss. A professional prophylaxis will not be administered. Subjects in Group III will receive semi-annual fluoride gel treatments as described for Groups I and II, except that no toothcleaning of any kind will be performed prior to treatment.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $65,547

1.0248, OPTIMAL METHODS OF ENAMEL REMINERALIZATION

W.I. Higuchi, University of Michigan, Ann Arbor Campus, School of Dentistry, *Ann Arbor, Michigan* 48104 (P50 DE 02731-130036)

Experiments conducted in these laboratories and many observations reported by others in the literature have recently led to the development of a model for the bahavior of hydroxyapatite and tooth enamel that features two distance sites from which dissolution can occur. This model has thus far been completely in accord with the observed demineralization and remineralization behavior of both hydroxyapatite and tooth enamel, and its properties are being thoroughly and quantitatively characterized in studies currently in progress in these laboratories.

The objective of the proposed project is to apply the fundamental knowledge being developed in these other projects to the design of practical and effective anti-caries treatments. One such treatment will consist of two steps, the first (and possibly the most important) of which is a pretreatment of ‘priming‘ in which mineral is removed in a carefully controlled manner resulting in an artificial lesion. This lesion, when given the appropriate remineralization treatment, will result in a tooth that is more caries resistant than either untreated sound enamel or sound enamel which has been given a remineralization treatment. The second type of treatment to be considered will consist of a single step, the remineralization of a naturally occurring carious lesion. Thus this project will recognize that both the nature of the starting lesion and the remineralization treatment influence the caries resistance of the treated tooth.

The project will therefore consist of two phases. Initially we will seek to establish criteria for the optimal composition of the tooth after remineralization and for the properties of the starting lesion that, when given the appropriate remineralization treatment, can lead to this optimally remineralized tooth. The second phase will be the development of practical means to achieve the desired clinical endpoint of caries-resistant teeth, either by the remineralization of naturally occurring lesions or by application of a two-step treatment to sound enamel.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $83,204

1.0249, FLUORIDE AND THE METABOLISM OF PLAQUE BACTERIA

S. Kashket, Forsyth Dental Center, Dept. of Chemistry, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 03917-05)

The ability of low levels of fluoride ions to protect teeth against the development of carious lesions is well known, although the mechanism by which the protective effect is exerted still is only poorly understood. It has been shown that fluoride can affect both the tooth enamel and the metabolism of acidogenic microorganism in plaque. Our interest has been in the latter and we have shown, in the early phase of this investigation, that low levels (1-10 ppm) of fluoride affect various strains of oral streptococci to differing degrees. It was suggested that such behavior of plaque microorganisms might explain the variability of clinical responses to water fluoridation. However, the basis for the variation in response to fluoride among the strains remained unexplained.

In subsequent studies we showed that cells of Streptococcus sanguis, S. mutans, S. salivarius and S. mitis strains can accumulate fluoride against a concentration gradient. Fluoride was bound within two distinct compartments within the cells, one with a low and the other with a high affinity constant. Gel chromatographic fractionation of the cytoplasms showed that numerous macromolecular binders exist within the cells, one of which appeared to be enolase. Purified enolases from these strains, however, exhibited essentially the same responses to added fluoride. It was concluded from this that fluoride sensitivity of the intact cells is not directly related to the properties of the cellular enolases.

It is expected that the information that will be gained from this study will help us to understand the basic biochemical events that give rise to the inhibition of bacterial metabolism by fluoride. This should enable us to determine why there are limitations to the clinical effectiveness of fluoride, and may lead to more effective approaches for the delivery of fluoride.

BIBLIOGRAPHIC REFERENCES: Kashket, S. and Bunick, F.J., Binding of fluoride in oral streptococci, Archs. Oral Biol. 23. 993-996 (1978). Kashket, S., Rodriguez, V.M. and Bunick, F.J., Inhibition of glucose utilization in oral streptococci by law concentrations of fluoride, Caries Res. 11, 301-307 (1977).

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $46,206

1.0250, SNF2 REACTION WITH APATITE AND OTHER CA/PO4 SYSTEMS

T.H. Jordan, Cornell College, School of Liberal Arts, Dept. of Chemistry, *Mount Vernon, Iowa* 52314 (R01 DE 04192-05)

Stannous fluoride has been shown to be an effective chemotherapeutic agent in combating tooth decay. While various mechanisms have been proposed to explain this anticavity action, only recently have we begun to learn what the actual products of the reaction between stannous fluoride and hydroxyapatite are. It is the objective of this project to extend the recent studies of this reaction system to low and high concentrations of stannous fluoride. In addition, the SnF_2 - $Ca(OH)_2$ - H_2O system will be studied. This system may provide a closer approximation to the oral environment than the stannous fluoride-apatite system does.

The products of these reactions will be identified by application of x-ray diffraction, infrared, atomic absorption, and wet chemical analytical methods.

BIBLIOGRAPHIC REFERENCES: The reaction of stannous fluoride and hydroxyapatite; F. David Babcock, Jeana C. King, and Truman H. Jordan; J. Dent. Res. 57, 933-938 (1978).

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $41,748

1.0251, KINETICS AND MECHANISMS OF ACTION OF FLUORIDES

J.S. Wefel, University of Iowa, School of Dentistry, Dept. of Pedodontics, *Jessup Hall, Iowa City, Iowa* 52240 (R01 DE 04486-02)

This grant proposal is designed to test several theories regarding the action of fluoride in reducing dental caries. By carefully elucidating the mechanisms whereby fluoride reduces dental decay, we may be able to develop more effective fluoride agents or treatment regimes. A multidisciplinary approach is being used in the work that includes chemical, morphological and histological evaluations of the reactions between various fluoride agents and sound or white spot enamel.

Initial experiments have concentrated on the effects of topical fluoride agents on enamel solubility, fluoride uptake and penetration as well as caries-like lesion formation after topical treatment. Since APF at 1.23% F seems to be the topical fluoride agent most used by the clinician, our topical fluoride studies have used this agent as a positive control. We are therefore evaluating the various fluoride treatment procedures by comparison to APF.

In this regard we have recently reported (IADR Abstract 0284) that APF applications to sound enamel produced greater fluoride uptake than titanium tetrafluoride. On the other hand TiF_4 applications afforded greater enamel solubility reductions than APF. Since these two in vitro criteria for assessing the possible anti-caries potential of preventive fluoride agents gave equivocal results, a third criteria was employed. The ability of the agents to prevent artificial lesion formation was the third criteria used. These studies showed that TiF_4 was a more effective agent in preventing artificial lesion formation than APF. Thus despite the higher concentrations of fluoride in enamel after APF treatment, the surface coating produced by the TiF_4 application afforded the enamel a greater degree of protection from lesion formation than APF. It would appear therefore that TiF_4 may be a more effective topical fluoride agent than APF in preventing dental decay.

BIBLIOGRAPHIC REFERENCES: J. S. Wefel, B. H. Clarkson, L. M. Silverstone, B. F. Zimmerman and M. J. Kastendieck Artificial Lesion Formation in TiF_4 and APF treated Enamel. J. Dental Research 58 Special Issue A, 0284, 1979.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $53,391

1.0252, IN VITRO MODEL FOR STUDY OF FLUORIDE ON TOOTH GERMS

G.E. Levenson, University of Pennsylvania, School of Dental Medicine, Dept. of Histology & Embryology, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (R01 DE 04686-02)

The overall objective is to establish an in vitro system to permit detailed study of fluoride, particularly at low levels, on developing mammalian tooth germs. Information will be sought at the light microscope and ultrastructural levels of effects of fluoride on ameloblasts, odontoblasts including developing stages. Cellular effects will be investigated in relation to effects on early dentinal and enamel matrix secretion as a response to fluoride. A primary aim is to investigate why ameloblasts are exquisitely sensitive to fluoride at doses as low as 1 ppm when considerably higher doses are required for observable effects in bone or other tissues. The advantage of this system is that it will permit study of fluoride at very low known doses in stages before mineralization, heretofore impossible in animals.

Principle objectives are to determine: (1) Observable effects at fluoride levels ranging downwards from 100 ppm. (2) The minimal duration required for fluoride activity at a range of fluoride levels.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$49,913

1.0253, REACTIONS OF TITANIUM FLUORIDE WITH HYDROXYAPATITE

T.H. Jordan, Cornell College, School of Liberal Arts, Dept. of Chemistry, *Mount Vernon, Iowa* 52314 (R01 DE 04705-01A1)

Topical application of titanium tetrafluoride has shown promise as an effective chemotherapeutic agent in combating tooth decay. The mechanism of action of such topically applied fluorides probably has both a chemical and a biological component. It is the objective of this project to investigate the chemical aspect of the mechanism of action of titanium tetrafluoride. The initial approach will be to study the reactions of titanium tetrafluoride with powdered hydroxyapatite in aqueous media. When the products of this reaction are identified, powdered dental enamel and enamel slabs will be treated with titanium tetrafluoride and the reaction products studied.

The products of these reactions will be identified by application of x-ray diffraction, infrared, atomic absorption, and wet chemical analytical methods.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$25,316

1.0254, ANTI-CARIES MECHANISMS OF FLUORIDE COMPLEXES - IN VITRO

B.H. Clarkson, University of Iowa, School of Dentistry, Dept. of Pedodontics, *Jessup Hall, Iowa City, Iowa* 52240 (R01 DE 04835-01A1)

Topically applied fluorides have only been partially effective in reducing caries. This study will investigate the effect of the pretreatment of enamel with polyvalent metal ions (iron (ferric), titanium and zirconium) as a means of increasing the efficacy of topical fluoride treatments. Teeth will be sectioned longitudinally into halves, one half will act as the test (pretreated) and the other as the control (APF treated). The experimental series will be divided into two phases: Phase A: The fluoride uptake from APF after pretreatment will be compared with the fluoride uptake from APF alone. In addition, the effect of this fluoride uptake on in vitro caries-like lesion formation will be determined.

Caries-like lesions, which are histologically indistinguishable from naturally occurring ones, will be produced using an acidified gel technique. The lesions from two adjacent sections, one test and one control, will be compared by carrying out inhibition studies in polarized light. Phase B: Attempts will be made to identify the products formed on and/or in surface enamel after the pretreatment regimen. This will help to establish the mechanisms by which a) polyvalent metal ions produce an elevated fluoride level in enamel, b) the pretreatments retard in vitro caries-like lesion formation. The techniques to be used in this phase of the work include polarised light microscopy, scanning electron microscopy and microprobe analysis. In this way, the changes in concentration and distribution of ions in enamel during lesion formation can be determined. Also, metal ions used as pretreatments (which inhibit lesion formation) will be combined with fluoride (e.g., $TiF4$) in a single solution. The effectiveness of this solution (as assessed in the dual experimental approach outlined above) will be compared with the corresponding metal ion pretreatment.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$56,075

1.0255, F DISTRIBUTION IN TEETH USING SILICATE CEMENT MODEL

R.W. Phillips, Indiana University, Indiana University - Purdue University at Indianapolis, School of Dentistry, Dept. of Dental Materials, *1121 W. Michigan St., Indianapolis, Indiana* 46202 (R01 DE 04904-02)

The objectives of this research are to: (1) obtain more complete definition of the mechanism by which silicate cement protects teeth against caries; and (2) use these data to explore the potential of incorporating the 'silicate mechanism' in other materials to provide anticariogenic properties. All the evidence indicates that the caries inhibiting ability of silicate cement is derived from fluoride incorporated during its manufacture. Research indicates that the fluoride, which slowly leaches from the material, acts upon both the hard tooth structure and the plaque. This study is concerned with obtaining more definitive information with respect to the effect on the tooth. It has been shown that the fluoride content of enamel is increased and its acid solubility reduced by direct contact with silicate cement. However, not only does less marginal caries occur in teeth restored with silicate than with other materials, but a lower caries incidence in other regions of the tooth and also in contact areas of adjacent teeth has been reported. This then implies more than a localized effect. Thus, this research proposes first to determine the effect of silicate restorations on the fluoride distribution in the enamel of the restored teeth. The restorations will be placed in extracted molar teeth. After periods ranging from 1 month to 1 year, the fluoride content of enamel biopsies taken from sites adjacent to the restorations and at other sites at prescribed distances from the restoration will be determined. Control data will be obtained from comparable tests using a fluoride-free silicate and also by biopsy of unrestored teeth. Using this same procedure, and the data obtained for silicate cement as a model, the potential anticariogenic properties of other materials which contain fluoride or to which fluoride has been added will be evaluated. These materials include silicophosphate cement, glass ionomer cement, acrylic and BIS GMA resins.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $61,140

1.0256, INTERACTION OF TOPICAL FLUORIDE WITH HUMAN ENAMEL

P. Gron, Forsyth Dental Center, Dept. of Chemistry, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 05067-02)

The aim of this research is to maximize fluorapatite formation in enamel from topical application of aqueous solutions of sodium monofluorophosphate and sodium fluoride. In the past year, we explored the effects of solution concentration, pH, application time, and acidic pretreatment of the enamel. Fluoride from sodium fluoride solutions penetrated more easily into the enamel than monofluorophosphate solutions under similar conditions. The former also produced more apatitically bound fluoride than the latter if an incubation period was allowed to follow the treatment, or if a prolonged application time was permitted. A monofluorophosphate solution was more efficient in effecting fluoride penetration and fluorapatite formation than a solution that contained the same amount of fluoride ion but no monofluorophosphate. Thus, the effect of monofluorophosphate interactions with enamel could not be explained solely as an action of the ionic fluoride present in the solution. Neutral and acidic sodium fluoride solutions buffered with phosphate or acetate gave much better results with respect to fluoride penetration and the amount of apatitically bound fluoride formed in depth as a result of a prolonged treatment time than did the monofluorophosphate solutions.

Work for the coming year will attempt to determine if effects of specific buffers are important for achieving high yields of apatitically bound fluoride, or, simply if maintenance of a stable pH can explain the findings. Other experiments will be concerned with surface active agents and their influence on the speed of fluoride interactions in depth as well as on the quantity and quality of reaction products. Finally, it is planned to explore the use of varnishes as potential sealants. Varnishes may function as diffusion barriers, thus enabling prolonged fluoride-enamel interaction and/or incubation period directly after treatment.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $77,396

1.0257, EXAMINATION IN CONNECTION WITH THE NATIONAL CARIES PROGRAM

M. Ringleberg, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Y01DE80028 (CONTRACT))

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0258, EFFECT OF DAILY AND WEEKLY RINSING WITH SODIUM FLUORIDE SOLUTIONS IN A NON-FLUORIDE AREA

S.B. Heifetz, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Community Programs Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00206-03)

In October 1976, a sodium fluoride (NaF) mouthrinse study was started in Biddeford, Maine, a non-fluoride area. Baseline dental examinations (DMFS Index) were made of 825 children in grades 5-7 attending seven schools in the community. Participants were randomly divided into three groups. Under teacher supervision, they rinse either weekly with a 0.2 percent NaF solution or a 0.1 percent sodium chloride solution (Placebo) or daily with a 0.05 percent NaF solution. Treatments are to be carried out for three school years. Follow-up dental examinations are scheduled annually to determine the anti-caries effectiveness of the two fluoride mouthrinse procedures. The third and last year of treatments was completed in June 1979. Final examinations will be made in October 1979.

BIBLIOGRAPHIC REFERENCES: Kingman, A., Heifetz, S.B. and Meyers, R.J.: A comparison of the anticaries effectiveness of daily and weekly rinsing with sodium fluoride solutions. In IADR Program and Abstracts of Papers: J. Dent. Res. 58:295, 1979.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $31,757

1.0259, COMPARISON OF DAILY AND WEEKLY RINSING WITH SODIUM FLUORIDE IN A FLUORIDATED COMMUNITY

W.S. Driscoll, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Community Programs Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00220-03 CPR)

The study was initiated in September 1977 with 1000 children in the seventh grade of nine junior high schools located in Des Moines, Iowa, community that has optimal amounts of fluoride in its supply of drinking water. The children were randomly assigned to one of the following three study groups: Group I (controls) rinse their mouths once every week in school for 60 seconds with a placebo solution; Group II follows an identical procedure using a 0.2% neutral sodium fluoride solution (0.09%F); Group III rinse their mouths once every day in school for 60 seconds using a 0.05% neutral sodium fluoride solution (0.023%F). The procedures are carried out under the classroom teacher's supervision for a period of three years. Baseline dental examinations, using the DMF surface index, were conducted in November 1977. The first follow-up examination was conducted in April 1979. Final examinations will be conducted in May 1980.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $34,171

1.0260, STUDY OF AN INTRAORAL DEVICE DESIGNED FOR PROVIDING SUSTAINED LOW LEVELS OF FLUORIDE

R.J. Shern, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Preventive Methods Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00262-01 CPR)

This investigation supplements earlier studies done by SRI in collaboration with Dr. Bowen and Dr. Mirth to develop a fluoride releasing device for intraoral use. The safety and pharmacokinetics of the device is being evaluated preliminary to possible clinical studies of its anticaries benefits. Preliminary studies in the subhuman primate suggest that the appliance will adhere to the teeth for releasing fluoride at the appropriate rate.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $54,246

1.0261, EFFECT OF CALCIUM GLYCEROPHOSPHATE AND FLUORIDE ON DENTAL CARIES IN RODENTS

W.M. Edgar, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00269-01 CPR)

Previous studies showing synergism between the effects of fluoride and calcium glycerophosphate in reducing dental caries in rats have been reinvestigated. Suboptimal levels of fluoride and calcium glycerophosphate gave a greater reduction in caries in combination than separately. Further statistical analysis will reveal whether or not this interaction is significant.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$6,548

1.0262, PREVENTION & CONTROL OF DENTAL DISEASE BY CHEMICAL ALTERATION OF TOOTH SURFACES

I.L. Shannon, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Oral Disease Research Laboratory, *2002 Holcombe Blvd., Houston, Texas* 77031 (580-006-P)

Laboratory and clinical research have led to the development of a professional and patient-applied regimen of fluoride treatment that brings a new level of protection against disease. High-risk patients (orthodontic patients, head and neck radiotherapy patients, patients with xerostomia of any etiology) are administered sequential topical treatments with 0.31% F-acidulated phosphate fluoride followed by 0.4% stannous fluoride. Fundamental to the provision of maximal protection is the daily (at bedtime) toothbrush application of 0.4% stannous fluoride gel by the patient. All three of these agents, as well as he treatment procedures, were developed in this laboratory; the products are manufactured here and distributed throughout the VA for use on veteran patients. Other areas of emphasis have been the importance of waterborne fluoride, systemic management of fluoride from the water and from oral dosage, response of the different types of tooth surfaces to fluoride treatments, and the place of fermentable carbohydrates (primarily simple sugars) in the etiology of dental disease.

BIBLIOGRAPHIC REFERENCES: Shannon, I.L. and Sanders, D.M. Urinary F Concentration in 6-9 Year Old Children Drinking Water with a Very Low F Level. Caries Research 13:18-22, 1979. Shannon, I.L., Edmonds, E.J. and Madsen, K.O. Honey: Sugar Content and Cariogenicity. J. Dent. Child. 46:29-34, 1979.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

1.0263, FIVE-YEAR COMPREHENSIVE PREVENTIVE DENTAL PROGRAM, BERMUDA

J. Weddup, Ministry of Health & Social Services, *Box 380, Hamilton 5, Bermuda*

Token fluoride scheme started in 1975 by Dr. Weddup, taken over by Kellogg Foundation, monitored by WHO/PAHO from August 1977 as a 5 year program. Financed on a yearly 20% diminishing.

No piped water necessitated tablet or liquid sodium fluoride. 'Parents consent only', 91% acceptancy obtained. Liquid - 6 months to years; tablet (0.75 mg) 3 years to 5 years, (1.0 mg) 5 years to 12 years. Nursery and primary teachers give daily dose - rinses conducted by Preventive Dental Staff consisting of 2 Preventive Dental nurses trained by Dr. Weddup.

Yearly surveys by PAHO of surface exams, enamel, saliva and urine analyses. Monthly oral hygiene visits to nurseries (40), primary schools (30) with tooth models, films (100) and slides/filmstrips by Preventive nurses. Publicity used: T.V., radio, news media, personal attendance, posters by local 5-12 year olds. Starting November 1979, sealant program for 6-7 year olds. Program did not actually start until September 1978, thus insufficient scientific data so far. Indications are that children with high fluoride content in enamel, saliva and urine are in low caries group.

Precise filing system with cross-reference facilities maintained by competent secretary/typist. Child population 12,500.

Second year shows higher acceptancy and lower refusal rates. Due to no dental service for under 5 year olds, Preventive Dental Officer will attend all nurseries with mobile equipment for examination and treatment.

SUPPORTED BY

W.K. Kellogg Foundation	funds n.a.

1.0264, EFFECT OF FLUORIDATION ON CHILDREN'S TEETH

Hardwick, University of Manchester, *Oxford Rd., Manchester M13 9PL, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$7,260

PREVENTION - FLUORIDE, INGESTED

1.0265, MAINTAIN SPECIAL MOUSE COLONY FOR FLUORIDE RESEARCH

L. Singer, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (N01DE92423 (CONTRACT))

Maintain a special mouse colony for fluoride research for the purpose of providing animals to qualified investigators. The animals will live on a defined fluoride intake (high and low levels) for at least five years, or approximately ten generations.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$19,800

1.0266. THE FLUORIDE CONTENT OF INFANT FOODS

L. Singer, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160070)

An extensive study to determine the total fluoride content of commercially prepared infant foods and the effect of the use of fluoridated water during processing on the fluoride content of these foods has been completed. Several major manufacturers of infant foods have supplied us with a full spectrum of infant foods produced at each of the domestic plants. Each sample was fully documented as to the fluoride content of the water used in processing. Our results show conclusively that the methods employed by other investigators (Pediatrics 55:517, 1975) will result in erroneously high fluoride values in certain infant foods. In addition, the use of fluoridated water during processing was shown to significantly increase the fluoride content of certain infant foods. The data indicates that the 'maximum' and 'minimum' total daily fluoride intake for infants up to 6 months of age is 0.127 mg and 0.010 mg of fluoride per kilogram of body weight, respectively.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$2,000

1.0267. THE FLUORIDE CONTENT OF INFANT, TODDLER AND ADULT FOODS

R.H. Ophaug, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160071)

In collaboration with the Food and Drug Administration, a study was initiated to determine the daily fluoride intake for infants and toddlers based upon analysis of 'Market Basket' food collections from four Dietary Regions of the United States. The results indicate a daily fluoride intake of 0.207-0.541 mg/day and 0.315-0.610 mg/day for infants and toddlers, respectively. On a body weight basis the daily fluoride intake for a 2-year-old child was directly related to the fluoride content of the water supply and was similar to, or less than, 0.05 mg/kg. Conversely, the daily fluoride intake for a 6 month-old infant ranged from 0.026-0.067 mg/kg and was not related to the fluoride content of the water supply.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$43,000

1.0268. EFFECT OF FLUORIDE ON IRON TRANSPORT

C.W. Carr, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160072)

We have previously shown that fluoride will reduce the severity of anemia in nursing mouse pups when the iron content of the maternal diet is low. (Proc. Soc. Exptl. Biol. Med. 153: 414, 1976). In vivo studies have provided evidence that fluoride exerts its effect by increasing the efficiency of iron absorption in the intestine. Results of an investigation of the movement of ferric iron (F ions) through electropositive membranes in the presence and absence of fluoride at pH 2 clearly indicate that fluoride increases the movement of Fe ions through electropositive membranes. On the basis of these data we have concluded that fluoride increases the diffusion of iron (Fe ions) through electropositive membranes by a passive mechanism involving the formation of iron-fluoride complexes which have less positive charge than Fe ions. We have recently found that in solutions (pH 4) initially containing 1 and 2 mM ferrous (Fe ions) sulfate the presence of 10 and 20 mM fluoride respectively, increases the permeability of the membrane to iron (Fe ions) manyfold.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$2,000

1.0269. METABOLIC HANDLING OF PERFLUOROOCTANOIC ACID

R.H. Ophaug, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160075)

Perfluorooctanoic acid has recently been identified as being a major form of nonionic fluorine in human serum. Using the oxygen bomb-reverse extraction technique developed in our laboratory, we achieve a recovery of 80% of the fluorine in perfluorooctanoic acid. This compares very favorably with a recovery of 15-20% obtained in an open ashing system. Adult female rats were administered a 2000 microgram dose of nonionic fluorine as perfluorooctanoic acid by stomach intubation and placed in metabolic cages for varying periods of time. The perfluorooctanoic acid is rapidly absorbed from the gastrointestinal tract and bound to serum proteins. Despite being bound to serum proteins, 89% of the nonionic fluorine was excreted in the urine after 96 hours. The remainder of the nonionic fluorine was excreted in the feces. The mechanism of excretion is currently being investigated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $30,000

1.0270, LONG TERM EFFECTS OF FLUORIDE INTAKE

L. Singer, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160078)

A colony of random bred Swiss-Webster mice have been maintained on a low fluoride (0.5 ppm or less) basal diet and drinking water containing 0 or 50 ppm of fluoride for approximately 10 years. This colony is being used for investigations of long term effects of fluoride intake on various biological parameters. There was no effect of fluoride intake on bone acid or alkaline phosphatase activity. The high fluoride mice, however, had serum alkaline phosphatase levels which were markedly higher than those of mice on low fluoride intake. In addition, the high fluoride mice excreted more sodium and potassium than the low fluoride animals.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $16,021

1.0271, EFFECT OF FLUORIDE INTAKE ON STR/N MICE

L. Singer, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160081)

Mice of the STR/N strain show evidence of a primary polydipsia and polyurea and undergo a progressive loss of alveolar bone with increasing age. A preliminary investigation with male STR/N mice indicates that providing the animals 50 ppm of fluoride in the drinking water results in a significant decrease in bone acid phosphatase and a significant increase in serum alkaline phosphatase. Due to severe hydronephrosis and the formation of an urethral plug, male mice of the STR/N strain are not suitable for long term studies. Additional studies, employing female STR/N mice, are being initiated to investigate the effect of fluoride intake on the progressive bone loss observed in these animals.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $13,000

1.0272, NONIONIC FLUORINE IN FOODS

L. Singer, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160082)

In 1976 Guy et al (ASC Symposium Series 23:7, 1976) reported that major portion of nonionic fluorine of human serum is composed of perfluorofatty acid derivatives containing 6-8 carbons. They speculated that there was widespread contamination of human tissues with these organic fluorocarbons and that they were derived from commercial sources. The food supply is a potential source of the organic fluorocarbons in human serum due either to the presence of native fluorocarbons in specific food items or to contamination of foods during packaging. Each composite in a 1977 adult 'market basket' food collection has been analyzed by methods which will detect the presence of organic fluorocarbons. Preliminary data indicate that Composite II (Meat, Fish, Poultry), Composite III (Grain and Cereal Products), Composite IV (Potatoes), and Composite VI (Legumes) may have significant quantities of nonionic fluorine.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,

best copy available

National Inst. of Health,
National Inst. of Dental
Research $5,000

1.0273, EFFECT OF FLUORIDE INTAKE ON THE LEVELS OF VITAMIN E IN SERUM AND SELECTED TISSUES OF GUINEA PIGS

G.T. Vatessari, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160083)

Based upon earlier studies showing a relationship between fluoride intake and serum cholesterol and triglyceride levels a study was initiated to study the effect of fluoride intake on the levels of vitamin E in the serum and liver of guinea pigs. The serum and liver of guinea pigs raised for 3, 6, 9 or 12 weeks on a high fat diet and drinking water containing either 0 or 25 ppm of fluoride were analyzed for total lipid and alpha-tocopherol. The values obtained varied greatly between animals and at no time was there a significant effect of fluoride intake on the 9 - 12 weeks, however, the alpha-tocopherol and total lipid content of the serum of high fluoride animals increased significantly; whereas that of the animals on low fluoride intake did not.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $5,000

1.0274, THE METABOLISM OF ISOLATED AMELOBLASTS

M.A. Crenshaw, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Pedodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130193)

Secretory ameloblasts are isolated by a sequential enzymatic digestion. Trypan blue vital staining and protein synthetic rates indicate that the isolated cells are viable.

The calcium transport kinetics of the isolated cells are being examined in terms of medium calcium, phosphate and fluoride concentrations. The effects of fluoride on respiration and protein synthesis are also being investigated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $47,042

1.0275, INFLUENCE OF ACID-BASE STATUS ON FLUORIDE METABOLISM

G.M. Whitford, Medical College of Georgia, School of Dentistry, Dept. of Oral Biology, *1459 Gwinnett St., Augusta, Georgia* 30902 (R01 DE 04332-04)

Results from studies proposed for the first three years of this grant have shown that urine pH is a major determinant of the renal clearance of fluoride. The rate is increased by an alkaline pH and depressed by an acid pH. These results are relevant to the cariostatic effect of fluoride because balance, and not merely intake, is the key variable. Other studies were completed and the results of these indicated that tramsmembrane pH gradients may be important in several aspects of fluoride metabolism and toxicity.

The studies proposed for the next three years will continue to explore the mechanism(s) of fluoride transport and distribution and the impact which variations in acid-base status and urine pH have on fluoride metabolism and toxicity. The characteristics of transport and distribution will be studied using red blood cells, the kidney and ureter, the oral mucosa and selected soft tissues. Two of the proposed studies will evaluate the effects of mild chronic acid-base disturbances induced by altitude and diet on the body-wide metabolism of fluoride in laboratory animals. Persons living at high altitudes exhibit a chronic respiratory alkalosis and should have a less positive fluoride balance than persons living at lower altitudes. Infants fed cows' milk based formulae tend to be acidotic, relative to breast-fed infants, and should exhibit a relatively positive fluoride balance.

Therefore, in addition to furthering our understanding of the characteristics and mechanisms of fluoride metabolism, these studies may reveal factors leading to the discovery of populations which require special consideration in terms of the amounts of fluoride provided them.

BIBLIOGRAPHIC REFERENCES: Whitford, G.M., and Stringer, G.I. Duration of the Fluoride-Induced Urinary Concentrating Defect in Rats. Proc. Soc. Expt. Biol. Med. 157: 44-49, 1978, in press. Whitford, G.M., and Pashley, D.H. Fluoride Metabolism and Body Fluid pH. In: Continuing Evaluation of the Use of Fluorides, AAAS Monograph, 1978, in press.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $56,390

1.0276, F BINDING BY EARLY ENAMEL MATRIX PROTEINS

J.W. Bawden, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Pedodontics, *Chapel Hill, North Carolina* 27514 (R01 DE 05289-01)

The general aim of the proposal is to investigate the functional aspects of the F ion binding to enamel matrix protein in order to gain additional insight into the mechanisms of fluoride action during the early stages of enamel formation.

It has been demonstrated, by four independent investigations, that the highest concentrations of F ion are found in newly deposited enamel matrix, rather than in the late maturing, rapidly mineralizing enamel where F ion incorporation into the apatite structure occurs. In bovine enamel, these high F ion concentrations in the early matrix appear to be the result of specific F ion binding by the matrix protein(s). Equilibrium dialysis experiments have shown that 40.7 (plus or minus 1.2) microns g F was bound per mg of matrix protein. A gel filtration elution profile showed that 18F is associated primarily with the second of four protein fractions.

The proposed study is designed to explore the functional aspects of F ion binding by early enamel matrix proteins. The specific aims are to: (1) establish the binding constants by flow dialysis methods using 18F; (2) compare the F ion binding capacities of late maturing enamel protein(s) and the early enamel matrix protein(s); (3) establish the Ca ions and HPO4 binding characteristics of the matrix protein by flow dialysis and study the effects of fluoride pre-loading on these parameters; (4) to characterize the binding mechanism(s); (5) use a tooth culture (in vitro) method to study the effect of F ion on 45Ca uptake in the early enamel matrix of developing rat molars; and (6) study the effect of F ion on the mineralization of early rat enamel matrix in vivo as measured by electron probe analysis.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$59,804

1.0277, THE EFFECT OF SCHOOL WATER FLUORIDATION ON DENTAL CARIES

S.B. Heifetz, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Community Programs Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00029-12 CPR)

Fluorides were added to the water supply of a school in Seagrove, North Carolina. The concentration of fluoride used was higher than the level considered optimal for community water fluoridation in the geographic area. Children attending the Seagrove school live in an area without a central water supply and where the various sources of well water contain negligible levels of fluoride. Children are exposed to the higher fluoride level only while at school in an attempt to approximate the total fluoride intake of children who drink optimally fluoridated water on a full-time basis. Baseline dental examinations for dental caries were made prior to the installation of fluoridation equipment. Follow-up examinations are conducted after four, eight, and twelve years to determine the extent of caries protection as increasingly larger segments of the study population become continuously exposed to fluoridated water at school since entering the first grade. Results of the four-year examinations showed appreciable decreases in caries prevalence compared with baseline findings. On the eight-year examinations, an assessment of the prevalence of dental fluorosis was made along with the regular examinations for dental caries. No children showed any definite signs of the condition. NIDR Classification: 10550.

BIBLIOGRAPHIC REFERENCES: Heifetz, S.B., Horowitz, H.S., and Driscoll, W.S.: Effect of school fluoridation on dental caries: results in Seagrove, N.C. after eight years. J. Amer. Dent. Assoc. 97:193-196, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$2,571

1.0278, EFFECTS OF CHEWABLE FLUORIDE TABLETS ON DENTAL CARIES IN SCHOOL CHILDREN

W.S. Driscoll, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Community Programs Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00032-11 CPR)

The study was initiated in October 1969 with 1034 children in the first and second grades of nine schools located in Wayne County, North Carolina, an area that has negligible amounts of fluoride (F) in its supplies of drinking water. Following baseline dental examinations, in which the DMF surface index was used, the children were stratified according to certain variables and then randomly assigned to one of the following three study groups: Group A (controls) chewed a placebo tablet, rinsed their teeth for 30 seconds with the resulting salivary solution, and then swallowed the material; Group B followed an identical procedure using an acidulated phosphate-fluoride (APF) tablet that contained 1 mg. F; Group C followed the same procedure as Group except that, after at least 3 hours, the procedure was repeated with a second APF tablet that also contained 1 mg. F. The procedures were carried out each day in school under the classroom teacher's supervision for a period of six years. Interim follow-up examinations were conducted in April 1972, May 1974, September 1975 and May 1977. Final examinations were conducted in May 1979.

BIBLIOGRAPHIC REFERENCES: Driscoll, W.S., Heifetz, S.B., and Korts, D.C.: Effect of Chewable Fluoride Tablets on Dental Caries in School Children: Results After Six Years of Use. J. Amer. Dent. Assoc. 97:820-824, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$15,274

1.0279, COMBINED SELF-APPLIED FLUORIDES FOR CARIES PREVENTION IN A NON-FLUORIDATED AREA

H.S. Horowitz, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Community Programs Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00070-07 CPR)

Baseline dental examinations were conducted in October 1972, on approximately 2200 children (grades K-12). All participants in grades K-6 chew daily in school under supervision an acidulated phosphate-fluoride (APF) tablet containing 1 mg. F, and swish and swallow the resulting solution. Once a week in school the same children also swish 10 milliliters of a 0.2 percent sodium fluoride solution for 60 seconds and then empty the contents of the mouth into a cup. A fluoride-containing dentifrice and toothbrushes are distributed to the same children for use at home. These combined preventive procedures will continue in the elementary schools for a minimum of ten years. Follow-up dental examinations are carried out biennially. Final examinations will be made in the fall of 1982 when all senior high school students will have participated continuously in the elementary school program since entering first grade. Children in the 7th grade of Nelson County's junior high school began to participate in the program in the fall of 1978. New grades will be brought into the program in junior high school on an incremental basis in future year.

BIBLIOGRAPHIC REFERENCES: Horowitz, H.S., Heifetz, S.B., Meyers, R.J., Driscoll, W.S. and Korts, D.C. Evaluation of a combination of self-administered fluoride procedures for the control of dental caries in a nonfluoride area: findings after four years. JADA, 98:219-223, February 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$39,744

1.0280, FLUORIDE EFFECT ON INCORPORATION OF RADIOACTIVE 45CA INTO HARD TISSUES OF DEVELOPING RAT TEETH

H.M. Stiles, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00117-06 CPR)

Pregnant rats were given intraperitoneal injections containing various concentrations of fluoride and 45Ca. Pups from these dams or pups injected similarly when they were 5, 9, or 12-30 days of age were sacrificed just prior to eruption of the first molars and their jaws were resected and teeth examined for radioactivity. A group of rat pups treated in the same manner using non-radioactive Ca were used to study the development of dental caries. In addition, a Ca blocking agent was used on one group of rats.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$15,382

1.0281, EFFECT OF SCHOOL WATER FLUORIDATION AND FLUORIDE MOUTHRINSING ON DENTAL CARIES

R.J. Meyers, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Community Programs Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00164-04 CPR)

About 1500 children attending grades K through 12 at five schools in Duplin County, North

Carolina, are exposed to fluoridation of the school water supply at four and one-half times the level estimated to be optimum for community fluoridation in the same geographic area. In addition, weekly mouthrinsing with a 0.2 percent NaF solution is done by children in kindergarten through the eighth grade. Teachers dispense 10 millimeters of solution to each participant-child and supervise the one-minute rinsing procedure which is carried out in the classroom. To evaluate the long-term benefits of the combined treatments on the prevalence of dental caries, pre-treatment clinical data will be compared with the data obtained every two years until the completion of the program in 1987. Baseline examinations using the DMF tooth and surface index were conducted in October/November 1975. The project is in its fifth year. The second follow-up examination will be made in September 1979.

BIBLIOGRAPHIC REFERENCES: Meyers, R.J., Driscoll, W.S., Murphy, R.F., Brunelle, J.A., and Horowitz, H.S.: Effect of school water fluoridation and fluoride mouthrinsing on dental caries: results after two years. Abstracted, IADR Program and Abstracts of Papers: J. Dent. Res. 58: 294, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$11,349

1.0282, PLAQUE VARIATIONS IN POPULATIONS INGESTING DIFFERENT LEVELS OF WATER FLUORIDE

H.M. Stiles, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00229-03 CPR)

Three communities having 0.3, 2.0 and 4.1 ppm fluoride in the drinking water were chosen as study sites. Children 12-18 years of age who had been lifelong residents in the sites comprised the populations. Plaque and saliva samples, collected from each participant, will be analyzed for microbial and fluoride content. DMF surfaces were also recorded for each participant. Data will consist of comparisons of various parameters among the three groups.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$56,073

1.0283, THE EFFECT ON DENTAL CARIES OF VARYING PERIODS OF SCHOOL WATER FLUORIDATION

S.B. Heifetz, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Community Programs Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00256-01)

Fluoride will be added to the water supplies of public schools in three Virginia counties to study the anti-caries effectiveness of fluoride ingestion: throughout grades K-6 (Cumberland Co.); throughout grades K-8 (Matthews Co.); and, throughout grades K-12 (Amelia Co.). All school populations live in areas that have no central water supplies and where drinking waters contain negligible concentrations of fluoride. In May, 1979, baseline dental examinations (DMFS Index) were made of a total of approximately 4,600 students in grades K-12 in the three counties. In September, 1979, schools containing the required grade levels for study fluoridated at a concentration of 4.5 times that recommended for community fluoridation in the geographic area. Follow-up examinations will be conducted after 3, 7, 9, and 13 years of study as increasingly more subjects become continuously exposed to fluoridated water at school for the desired periods of time.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$18,548

1.0284, BIOLOGICAL TESTING OF FLUORIDE

G.R. Martin, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00275-01 DB)

The purpose of this project is to study the action of fluoride on various systems used to detect clastogenic or mutagenic substances. To date fluoride has been examined in microbiological assays used to detect mutagens and found to be non mutagenic. No effects on chromosome structure were noted in animals given widely different levels of fluorides. DNA repair after X-ray was unchanged by fluoride. No genetic effects of fluoride were noted in a recessive lethal test of fluoride on drosophila. The data indicate that fluoride has no mutagenic activity.

BIBLIOGRAPHIC REFERENCES: Martin, G.R., Brown, K.S., Mathison, D., Lebowitz, H., Singer, L.

and Ophaug, R.: Chromosome aberrations in mice and mutations in microorganisms are unaffected by fluoride exposure. Mutation Research, 66: 159-167, 1978. Kram, D., Schneider, E.L., Singer, L., and Martin, G.R.: The effects of high and low fluoride diets on the frequencies of sister chromatid exchanges. Mutation Research, 57: 51-55, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$8,748

1.0285, STUDY OF DENTAL EFFECTS IN A POPULATION EXPOSED TO H2O FLUORIDE LEVELS IN 'CRITICAL' ZONE

C.T. Smith, University of Texas, Health Science Center at San Antonio, School of Dentistry, *San Antonio, Texas* 78284 (D823B-024C)

OBJECTIVE: In the proposed study, information regarding mottling and discoloration of teeth will be compared to fluoride levels in the public water supplies of several communities. Volunteer participants will be recruited through public schools in eight communities having naturally occurring high fluoride levels. Students from grades 1-4 (6-9 yrs of age) and whose families utilize water delivered by the community water system will serve as a source of volunteers.

APPROACH: An oral examination to determine level of mottling, discoloration of teeth and a DMFS Survey will be administered to each participant and a urine sample will be collected for fluoride analysis. Information regarding personal and health background will be obtained with specially designed questionnaire forms. An opinion survey regarding perception of problems related to teeth mottling and discoloration will also be administered by use of a second questionnaire form. Data resulting from oral examinations, analyses of urine samples, background health and personal indicators, and opinions regarding the problems of mottling and discoloration will be compared to fluoride levels in the various community water supplies to determine the specific level of fluoride at which problems occur.

SUPPORTED BY

U.S. Environmental Protection Agency, Office of Research & Development, Health Effects Research Lab.	$168,000

PREVENTION - OTHER TRACE MINERALS

1.0286, THE EFFECT OF FLUORIDE ON ACUTE ZINC DEFICIENCY IN THE RAT

L. Singer, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160079)

An investigation has been initiated to study the mobilization of bone zinc during periods of acute dietary zinc deficiency and to determine if the fluoride content of the bone influences the mobilization of zinc. Bone alkaline phosphatase activity was reduced in the zinc deficient animals when compared to pair-fed control animals. Bone alkaline and acid phosphatase activity of the ad libitum-fed group was significantly higher than the levels observed in either the pair-fed or zinc-deficient groups and is probably a reflection of decreased food consumption in the latter animals. A 4-week period of zinc deficiency resulted in a progressive increase in the urinary pMoles cAMP/micrograms creatinine ratio and in the mobilization of skeletal zinc in young, growing animals. The pMoles cAMP/micrograms creatinine ratio returned to the control values 36 hours following zinc repletion. In contrast, adult animals exhibited no mobilization of skeletal zinc during a 10-week period of zinc deficiency and the pMoles cAMP/micrograms creatinine ratio in the urine was not significantly elevated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$11,900

1.0287, STRENGTH OF POLYMERS IN TOOTH RESTORATIVE MATERIALS

D.T. Turner, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Operative Dentistry, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130149)

The overall aim of the research is to provide information which will help with evaluation of polymeric materials in dental applications. The specific objective is to investigate the relationship between the structure and properties of dental polymers made from mixtures of polymeric powder and monomer. These materials are not mechanically strong but are important because they can be processed in vitro in teeth restoration, bone prostheses, etc. The work includes studies of the strength of polymethyl methacrylate characterized with respect to primary molecular weight and crosslink density. The main emphasis is on tooth restorative materials cured by exposure to ultraviolet light. Future work will concentrate on polymers made from dimethacrylates and other monomers currently used in tooth restorative composite materials.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$28,136

1.0288, FLUORIDE-SELENIUM INTERACTION IN DENTAL CARIES

T.R. Shearer, Oregon State Higher Education System, University of Oregon Health Sciences Center, School of Dentistry, Dept. of Biochemistry, *611 S.W. Campus Dr., Portland, Oregon* 97201 (R01 DE 03856-06)

The overall objective of the total project is to test if fluroide and selenium interact in dental tissues. This is designed to provide basis for the cariogenic nature of selenium. Current studies have been directed towards measuring if different dose levels: 50, 100 and 150 microns Se/day, I.P., alter the uptake of simultaneously injected fluoride into the calcifying region of the rat incisor. No effect has been found, leading to the tentative conclusion that selenium may be caries-promoting without influencing the uptake of fluoride into enamel.

BIBLIOGRAPHIC REFERENCES: Shearer, T.R., Lis, E.W., Johnson, K.S., Johnson, J.R. and Prescott, G.H. 1978. Zinc Concentrations in the Amniotic Fluid of High Risk Pregnant Women. Nutr. Rept. Int., in press. Johnson J.R. and Shearer, T.R. 1978. Selenium Uptake Into Teeth Determined by Fluorimetry, in press. J. Dent. Res.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$32,212

1.0289, TRACE ELEMENT INFLUENCE ON CARIES IN VITRO

M.F. Little, Eastman Dental Center, *800 Main St. E., Rochester, New York* 14603 (R01 DE 04431-03)

The production and remineralization of artificial white spots in human enamel in vitro has been accomplished using a layering technique consisting of gel impregnated fiberglass meshes on the enamel which is exposed to lactic acid and then to remineralizing solutions. It will be the objective to ascertain the best level of Ca and P, F and Sr as well as pH for increasing the rate of remineralization. The resistance of that enamel to a second demineralization will be assessed. The level of mineral within the layers of meshes during the processess will be treated mathematically to determine if the laws of diffusion are adhered to.

BIBLIOGRAPHIC REFERENCES: Little, M.F. and Baer, J.E. Ion gradient in 'plaque' covered in vitro white spots of enamel. J. Dent. Res. 56:A154 (Abst. 0446), 1977. Little, M.F. and Baer, J.E. Remineralization pattern in in vitro induced white spots. J. Dent. Res. 57:A88, (Abst. 054), 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0290, EFFECTS OF MATERNAL ZINC DEFICIENCY ON ENAMEL ZINC

F.A. Catalanotto, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Pediatric Dentistry, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 04830-02)

The etiology of a large number of birth defects is unknown and probably multifactorial. Maternal zinc deficiency has been implicated as a causative factor in several birth defects. However, at the time of diagnosis of the birth defect, if is usually difficult, if not impossible, to determine the adequacy of the maternal zinc status during the development of the malformed embryonic parts. This project will attempt to demonstrate maternal zinc deficiency by studying the zinc content of tooth enamel formed during embryonic life. After preliminary animal studies on tooth enamel from rats fed zinc deficient diets, we will section exfoliated primary teeth of healthy control subjects and subjects with congenital anomalies, i.e., cleft lip and/or palate and spina bifida. The sectioning will be done in such a manner as to separate out fragments of enamel that calcified at approximately the same time as the development of the embryonic organs of interest. We will then examine the zinc content of the tooth enamel using atomic absorption spectrophotometry. We will analyze for differences within individual teeth as well as between groups of subjects.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,

National Inst. of Dental
Research $25,968

1.0291, BIOCHEMICAL ROLE OF ZINC IN TEETH AND BONES

H.S. Hsieh, University of Alabama in Birmingham, School of Dentistry, Institute of Dental Research, *1919 7th Ave. S., Birmingham, Alabama* 35233 (R23 DE 05037-01)

Zinc deficiency in growing individuals results in abnormal bone growth. This proposal described the application of two useful approaches to the study of the nutritional effects of zinc deficiency on the formation of bones. The first approach involves the use of a nylon tube implanted into the aveolar cavity of the mandibular incisor of guinea pigs, from which a purely zinc-deficient bone can be obtained in a zinc depleted animal. The second approach is to culture rat calvaria in medium containing either zinc deficient or adequate rat serum, which serves as a convenient alternative for nutritional depletion studies in animal models. The uptake of radioactivity labeled precursors of the components of organic matrix of the bone will then be evaluated in vivo and in vitro. Emphasis will be placed on the metabolism of glycosaminoglycans (GAG's), since GAG's are important components of the organic matric and previous studies indicate that major alterations in GAG composition take place in Zn deficient bones.

The effect of zinc on another calcified tissue, the tooth, has received only limited attention. This proposal also describes the use of two model systems (rat teeth and caries models) to examine the effect of zinc deficiency on developing teeth. Attempts will be correlate their structural and biochemical changes with the susceptibility to dental caries. This will be done by challenging zinc deficient rat pups, which are born to and nursed by marginally zinc-deficient rat dams, with Streptococcus mutans and a caries promoting diet.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $25,095

1.0292, THE MODIFICATION OF THE MICROBIAL FLORA OF THE DENTAL PLAQUE BY TRACE ELEMENTS

G. Colman, Royal College of Surgeons of England, Dental Research Unit, *35/43 Lincolns Inn Fields, London, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY
Medical Research Council $24,210

PREVENTION - IMMUNIZATION

1.0293, STUDY OF IMMUNIZATION TO CARIES

D.D. Boyd, Hazleton Lab. America Inc., *9200 Leesburg Tpke., Vienna, Virginia* 22180 (N01DE42434 (CONTRACT))

The Contractor will provide 40-50 Macaca fascicularis monkeys approximately sixteen months of age. The Contractor would house and maintain the monkeys with suitable sterility and safety procedures for period of not less than two years. The monkeys would be fed eight times daily and less frequently on weekends with a special caries-conducive diet which would be specified by NIDR. The Contractor would also provide facilities for clinical (general anesthesia and minor oral surgery) and radiographic examinations.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $177,478

1.0294, IMMUNOLOGIC CROSS-REACTIVITY OF ORAL STREPTOCOCCI

R.J. Nisengard, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Periodontology & Endodontics, *3435 Main St., Buffalo, New York* 14214 (N01DE62488 (CONTRACT))

This research study shall be conducted to study the immunologic cross-reactivity of oral streptococcal antigens with mammalian tissue and tissue compounds. The contractor shall be required to collect representative strains of oral streptococci. The contractor shall be required to obtain sera from rheumatic fever patients and heart tissues from autopsy of cases with rheumatic fever as a diagnosed component of their medical history. Delineate the streptococcal antigenic determinants responsible for any binding to tissue by extracting and fractionating, by suitable means, whole cells of the indicated immunoreactive streptococci.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $15,717

1.0295, PRODUCTION OF SPECIFIC ANTISERA

R.W. Newcomb, University of Chicago, School of Medicine, Dept. of Pediatrics, *5801 S. Ellis Ave., Chicago, Illinois* 60637 (N01DE72406 (CONTRACT))

Produce high titer antisera to rat or monkey proteins with specificity as follows: goat anti-IgA will react with IgA, but not (by tests defined) with IgG, IgM, or other serum or exocrine fluid proteins; goat anti-a chain will react with IgA, but not with IgG, IgM, immunoglobulin light chains, or other serum or exocrine fluid proteins; goat anti-sIgA will react with IgA from serum and exocrine sources and probably with SC, but will not react with IgG, IgM, immunoglobulin light chains, or other colostral or salivary proteins; goat anti-IgM will react with IgM, but not with IgG, IgA, or other serum proteins; and goat anti-u chain will react with IgM, but not with IgG, IgA, immunoglobulin light chains or other serum proteins.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0296, SALIVARY ANTIBODIES TO S. MUTANS - INDUCTION AND EFFECTS

R.T. Evans, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (R01 DE 04061-05)

Past experiments have shown that monkeys (Macaca fascicularis) immunized directly into the parotid glands with a formalin-killed whole cell vaccine of Streptococcus mutans develop secretory antibodies (sIgA) in their saliva. These antibodies inhibit the colonization of the tooth when viable S. mutans organisms, the same as the immunizing strain, are implanted in the oral cavity.

The objectives of this research proposal are: (1) to immunize monkeys with purified antigens from S. mutans serotypes c and d which have been shown by in vitro assays to inhibit bacterial adherence, (2) to characterize the serum and salivary immune response to these purified antigens using immunofluorescent and enzyme-linked immunosorbent assays, and (3) to examine the effects of immunization on infectivity and caries induction by S. mutans in monkeys. Emphasis will be placed on determining the oral-parenteral immunization route that results in a strong, prolonged sIgA response in saliva.

Antigens to be examined are glucosyltransferases, serotype specific polysaccharides, glucan-binding proteins (receptors), and cell-associated glucans.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $147,741

1.0297, SECRETORY IMMUNE RESPONSE AND S. MUTANS ENZYME ANTIGENS

M.A. Taubman, Forsyth Dental Center, Dept. of Immunology, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 04733-03)

This research will seek to develop an immunologic basis for the selection of GTF enzymes from Streptococcus mutans which will induce protection against dental caries in rodents caused by commonly encountered serotypes of this microorganism. Procedures will be performed, primarily in rats, to delineate both immunologic parameters of the secretory (esp. salivary) immune responses and the function of these salivary immune responses in protecting the animals from experimentally induced dental caries. Animals will be immunized with crude and defined enzyme antigens from S. mutans and the induction of antibody will be assessed by functional inhibition and radioactive GTF binding assays.

The parameters of the secretory immune response to be studied include: relative affinity, relative avidity, maturation, duration, anamnesis, priming, and T-cell dependence of secretory antibody. Factors influencing the kinetics, anamnesis, and priming of immunocompetent cells in the salivary glands will also be investigated. Relative affinity and avidity of secretory antibody will be determined using the haptenated bacteriophage neutralization inhibition technique. Antibody activity of different Ig classes will be determined by sensitive hapten binding techniques. A combined immunofluorescence technique will be used to detect antibody-forming cells in salivary glands.

The antigen preparations and immunization protocols will be integrated to develop conditions which might be eventually feasible for use in humans.

BIBLIOGRAPHIC REFERENCES: Daniel J. Smith, Martin A. Taubman and Jeffrey L. Ebersole (1979). Preparation of glucosyltransferase from Streptococcus mutans by elution from water-insoluble polysaccharide with a dissociating solvent. Infection and Immunity 23: 446-452. Jeffrey L. Ebersole, Martin A. Taubman and Daniel J. Smith

(1979). The effect of neonatal thymectomy on the level of salivary and serum immunoglobulins in rats. Immunology 36: 649-657.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$116,327

1.0298, SYMPOSIUM AND WORKSHOP ON ANIMAL MODELS IN CARIOLOGY

J.M. Tanzer, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Oral Diagnosis, *Farmington Ave., Farmington, Connecticut* 06032 (R13 DE 05389-01)

This application is for support of the convening and conduct of a Symposium and Workshop on experimental animal models and their applications to caries research. The importance of such a meeting is indicated by the need for clarification of the state-of-the-art concerning animal models in caries research and for dissemination of such information to both present and prospective experimental cariologists. The Symposium and Workshop format is proposed as the method for addressing these general objectives. Acknowledged authorities on various topics of interest will be invited to participate in this meeting by presentation of formal talks and papers and by participation in the discussions of the meeting. In addition, a small group of the participants will be invited to participate further in a Workshop session which will attempt to summarize and crystallize current thinking with respect to the topics deliberated upon during the Symposium. Among the topics for specific discussion during the Symposium will be a historical review of animal models of human diseases and specifically the history of their use in study of dental caries, impact of regulatory agencies and groups on animal experimentation, care of caries test animal models prior to experimentation, evaluation of the microbiological status of animals, husbandry during experiments, characteristics and applications of specific animal models in study of caries, experimental strategies and objectives, lesion and plaque scoring, cariogenic flora and infection, animal diet composition and regulation of feeding, comparative salivary composition of animal models, special techniques in animal model caries experiments, and anticaries agent testing. The Workshop session will not only attempt summary of the 'state-of-the-science' but will address the issues of 1) relevance of animal models to human caries and its control, 2) summary of pitfalls in study of caries using experimental animals, and 3) directions for future research and identification of important problems. The proceedings of the Symposium and Workshop will be rapidly published and widely distributed to the most relevant scientific community.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$45,280

1.0299, DEVELOPMENT OF IMMUNITY TO CARIOGENIC STREP

B.A. Peri, University of Chicago, School of Medicine, Dept. of Pediatrics, *5801 S. Ellis Ave., Chicago, Illinois* 60637 (R23 DE 04771-03)

Interaction of genetic and environmental factors regulating the immune response to environmental antigens on mucosal surfaces is being studied. The influence of exposure to cariogenic bacteria at various ages and by various routes on amount and isotype of antibody is emphasized.

The model system used is based on our published observations that inbred Harvard caries-resistant (HCR) rats differ from the Harvard caries-susceptible (HCS) rats in their immune response to cariogenic Streptococcus faecalis ND547 (S.F.). We have independently tested the environmental variables that appear to influence this difference to identify a factor regulating antibody production in the gnotobiotic HCR rat. Dental caries incidence correlates well with changes in bacterial agglutinin titer, induced by mucosal associated antigen in this model. Identification of immunoglobulin class of specific antibody should help to define the mechanism of observed differences in responses and the possible protective role of secretory antibody and the mucosal immune response. We also will look for differences in maturation of Pcyeis patches in the two rat strains under various gnotobiotic environments.

BIBLIOGRAPHIC REFERENCES: Peri, B.A. and Wagner, M. 1977. Immune Response and Dental Caries Incidence in Streptococcus faecalis - Monoassociated Harvard Caries-resistant and Caries susceptible Rats. Infect. Immun. 16:805-811.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$27,464

1.0300, A RIBOSOMAL VACCINE AGAINST DENTAL CARIES

J.J. Bozzola, Medical College of Pennsylvania, School of Medicine, Dept. of Microbiology, *3300 Henry Ave., Philadelphia, Pennsylvania* 19129 (R23 DE 05039-02)

It is proposed to investigate ribosomal preparations from Streptococcus mutans for use in the anticaries vaccine. Ribosome-enriched fractions will be obtained from strain GS-5 and biochemically analyzed as to content. The material will be injected into rabbits solely, as well as in combination with purified glucosytransferase (GTF) enzymes, and antisera will be characterized for ability to: adhere to and agglutinate serotype c cells, prevent adherence of the bacteria, inhibit GTF activity, react with mammalian tissues and provide cross-serotype of protection. After the nature of the immunogen and antibody response has been determined in rabbits, the ability of the vaccine to prevent dental caries will be tested in rats.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $30,063

1.0301, IMMUNOLOGICAL STUDIES - CARIES AND PERIODONTAL DISEASE

J. Haber, Tufts University, Boston Campus, School of Dental Medicine, Dept. of Periodontology, *136 Harrison Ave., Boston, Massachusetts* 02111 (R23 DE 05240-01)

Present information suggests that host immune responses to specific oral microorganisms play an important role in caries and peridontal disease. It is not clear whether this role is protective or destructive. Animal studies indicating that, in caries, the host salivary IgA response can be protective in nature, have prompted continued efforts to develop a caries vaccine. The purpose of the proposed research is to determine which combination of strain, antigen dose, and route of immunization results in optimal stimulation of the salivary IgA response in mice, and to characterize the cellular events underlying this secretory immune response. A sensitive radioimmunoassay will be used to quantitate specific antibody molecules in six immunoglobulin classes directed against sheep red blood cell surface antigens. Experiments using genetically defined inbred, hybrid, and backcross mice and oral administration of antigen will determine the number of genes involved and the nature of genetic control of secretory immune responsiveness. The effects of route of immunization will be studied by immunizing groups of animal parenterally, orally, intra-gastrically, and by injection of the salivary glands and Peyer's patches. Appropriate dose-response studies will be included. The source of salivary Iga precursor cells will be studied in a cell transfer system, in which sensitized Peyer's patch and mesenteric lymph node cells will be transferred to normal, syngeneic recipients, whose saliva will be tested for Iga antibody. The potential regulatory relationships between the secretory and systemic immune systems will be defined in a passive antibody transfer system. It is hoped that this research will contribute to the development of an effective caries vaccine, and a better understanding of the role of the host immune response in peridontal disease.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $32,438

1.0302, DEVELOPMENT OF AN ANTI-CARIES VACCINE

W.H. Bowen, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00081-06 CPR)

A colony of primates, Macaca fascisularis, which has been infected with Strep. mutans and is being fed a diet rich in sucrose is being used to develop a vaccine against dental caries. Pneumococcal polysaccharides types II and IX, glucosyl transferase, and heat killed Strep. mutans cells have been administered to age matched monkeys intraductally or intramucosally with aluminum hydroxide as adjuvant. No protection was observed in the monkeys vaccinated using the pneumococcal polysaccharide or in the animals vaccinated intramucosally. Monkeys vaccinated with glucosyl transferase had fewer lesions than the other animals.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $24,917

1.0303, PURIFICATION OF RAT IMMUNOGLOBULINS

M.F. Cole, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Preventive Methods Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00236-02 CPR)

Immunoglobulins M and G (IgM and IgG) were purified from rat serum and secretory IgA from rat colostrum by molecular sieve, ion exchange and affinity chromatography. Purification of IgM was complicated by contamination with alpha 2, macroglobulin.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $25,759

1.0304, GROWTH ENERGENICS AND INTERACTION OF PLAQUE MICROORGANISMS

S.A. Robrish, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00243-02 CPR)

Pure cultures of bacteria were prepared under highly controlled conditions to be used as antigens for a variety of immunologic experiments. Antigens are to be prepared to be used for antiserum preparation to quantitate Streptococcus mutans and Streptococcus sanguis in mixed culture. Experiments have continued on the growth properties of S. mutans and S. sanguis in batch and continuous modes.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $27,720

1.0305, ANTIBODY RESPONSE IN HUMANS TO STREP. MUTANS

W.H. Bowen, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Etiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00267-01 CPR)

This study was carried out to determine whether humans would develop serum and salivary antibodies after swallowing large doses of Strep. mutans in enteric coated capsules. It was observed that it was easier to infect those humans who harbored Strep. mutans than those who were mutans-free. Antibodies were found in saliva and serum following vaccination per os.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $18,630

1.0306, ANTIGENS RESPONSIBLE FOR NATURALLY OCCURRING ANTIBODIES TO S MUTANS IN HUMAN SERA AND SALIVA

M. Levine, University of Oklahoma, Health Science Center, School of Medicine, Dept. of Biochemistry & Molecular Biology, *Box 26901, Oklahoma City, Oklahoma* 73190 (SA 107377)

Dental caries and periodontal disease are caused by bacterial plaque accumulating to teeth. These accumulations were found to contain at least two chemically and serologically different, soluble antigens to which many human sera showed precipitin reactions. The precipitins were markedly inhibited by pre-treatment with Staphylococcal Protein A which removes IgG. The antigens were found in cell pellet and culture filtrate preparations from many oral bacteria: one from Actinomyces spp. and the other common to Streptococci, Lactobacilli, and Staphylococci spp. All subjects reacted to the former antigen (A positive), the latter (S positive), both (A positive S positive), or neither (A negative S negative). Strongly reactive A positive and S positive sera were used in electroimmunoassay to help isolate the respective antigens from column effluents for study of their chemical nature. The S positive antibody determinant is apparently alkali-labile D-alanyl esters of glycerol teichoic acid. S positive subjects had a history of brushing their teeth significantly less often than S negative subjects. Unlike the latter in whom caries severity correlated significantly with age between 20 and 35 (P less than 0.01), S positive subjects showed no correlation (P approximately equal to 0.50). A positive subjects from fluoridated areas had significantly less caries than A negative subjects and A positive S negative subjects had the fastest rate of caries increase with age.

SUPPORTED BY
(No Supporting Organization
Reported) $10,700

1.0307, CENTRAL AND PERIPHERAL IMMUNOLOGICAL CONTROL IN THE PREVENTION OF DENTAL CARIES

T. Lehner, University of London, Guys Hospital Medical School, Dept. of Oral Immunology & Microbiology, *London Bridge, London SE1 9RT, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY
Medical Research Council $17,562

1.0308, RESEARCH INTO THE REDUCTION OF DENTAL CARIES BY IMMUNIZATION

B. Cohen, Royal College of Surgeons of England, *35/43 Lincolns Inn Fields, London, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY
Medical Research Council $1,168,535

1.0309, SEROTYPING OF STR. MUTANS IN COMMUNITIES

L.C. leRoux, University of Stellenbosch, Research Group in Dental Epidemiology, Oral Pathology, *Private Bag 11, c/o Prof. C.W. VanWyk, Tygerberg 7505, Cape Province, South Africa*

The serotyping of Str. mutans obtained from special communities. Str. mutans is isolated from plaque of persons from special secluded communities and serotyped.

Antisera is being prepared.

SUPPORTED BY
South African Medical Research Council $3,000

PREVENTION - HYGIENE, GENERAL

1.0310, USE AND EFFECTIVENESS OF A COATED, ELASTOMERIC DENTAL RIBBON COMPARED TO CONVENTIONAL DENTAL FLOSS

J. Alexander, Cooper Lab. Inc., Research & Development Division, *110 E. Hanover Ave., Cedar Knolls, New Jersey* 07927 (DAMD17 78 C 8084)

Initiate new modality of providing better oral hygiene for the soldier in the field.

A new elastomeric ribbon with an adhesive coating will be compared to conventional floss and toothbrush methods of personal oral hygine to determine a comparative effectiveness. An addition to accepted visual measurement methods, results will be evaluated by SEM and QIAC methods.

SUPPORTED BY
U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research $26,692

PREVENTION - MOTIVATION

1.0311, COMPLIANCE FACTORS IN CARIES PREVENTION

M.K. Nikias, Columbia University, College of Physicians & Surgeons, Dept. of Public Health, *630 W. 168th St., New York, New York* 10032 (R01 DE 04303-03)

This study will determine: the extent to which people comply with caries prevention procedures and maintain compliance behavior over time; and the extent to which compliance is related to characteristics of the patient and his milieu, of the regimen and of the dental setting. It will also examine the relationship of these factors and of degree of compliance behavior to oral status.

Data will be collected by home visit interviews from patients who have completed recognized and professionally defined preventive dentistry programs at private offices of dentists.

In each case assessments will be made of performance of prescribed procedures and oral status by observation; reported compliance, social psychological and demographic characteristics of patients, characteristics of the regimen, of the dental setting, and of the communication approach will be determined from the interview and other sources.

These data will be analyzed to see what factors and processes predict compliance and develop a typology of compliers. The study will be valuable for improving existing caries preventive programs and for designing the kind of appeal that may increase compliance to carries prevention programs.

SUPPORTED BY
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $119,547

1.0312, VA COOPERATIVE STUDY NO. 59 - PATIENT COMPLIANCE AND ITS ROLE IN DENTAL PLAQUE CONTROL

R.E. Morhart, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *1201 Northwest 16th St., Miami, Florida* 33125 (546-003-I)

The specific aim of this study is to evaluate the effect of an intervention model on long-term patient cooperation with proven effective dental health self-care techniques. It is a two-year longitudinal prospective study with all standardized measurements taken before, as well as various periods after interventions in both the experimental and control groups. The study population will be composed of 300 veterans (100 patients at three Veterans Administration Hospitals) randomized to either the experimental or control group. The measurements consists of: 1) a series of questionnaires which records the patient's prior dental experiences, relevant dental knowledge, and attitudes and beliefs about dental health (the belief dimensions comprise the elements of the Health Belief Model, HBM) and 2) an Oral Physiotherapy (OPT) Skill Index and five well-accepted dental health clinical indices which are used to determine compliance. The control groups will receive a traditional knowledge-oriented preventive dentistry intervention along with OPT skill development. The experimental group will receive OPT skill development and a tailored intervention (internality training). An educational diagnosis is performed on individuals in the experimental group based on results of their questionnaire which will identify deficiencies in attitudes and beliefs (HBM) that are below a level presumed necessary for compliance. We then intervene to specifically correct or modify any deficiencies that are found. Results of this study will determine not only how attitudes, beliefs, motives and concerns about dental health are related to long-term patient compliance with self-care dental health regimens but will determine also the alterability and durability of these dimensions.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

1.0313, IMPROVEMENT OF ORAL HYGIENE OF A GROUP OF CHRONICALLY REGRESSED SCHIZOPHRENIC PATIENTS BY USE OF A POSITIVE REINFORCEMENT PROGRAM

J.S. Gunderson, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Battle Creek, Michigan* 49016 (515-021-I)

This study proposes to investigate whether the oral hygiene of a group of schizophrenic patients can be changed by the use of positive reinforcement for the target behavior of improved toothbrushing and flossing.

This research is relevant to our mission since an active preventive dentistry program has become an integral part of the VA Dental Service mission.

The benefits of this study will be to determine if it is feasible to use a contingency management system to improve patient oral hygiene in a group of patients in which all other methods to improve their hygiene have failed.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

DEMONSTRATION

1.0314, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECT

H.L. Bailit, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Behavioral Sciences & Com Hlth, *Farmington Ave., Farmington, Connecticut* 06032 (N01DE52459 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

1.0315, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECTS

L.W. Ripa, State University of New York, Health Science Center at Stony Brook, School of Dentistry, Dept. of Childrens Dentistry, *Stony Brook, New York* 11790 (N01DE52460 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0316, COMMUNITY CARIES PREVENTIVE DEMONSTRATION PROGRAMS

P.F. Depaola, Forsyth Dental Center, *140 Fenway St., Boston, Massachusetts* 02115 (N01DE52461 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explore. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0317, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECT

D.H. Leverett, Eastman Dental Center, *800 Main St. E., Rochester, New York* 14603 (N01DE52462 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 is treated, K-9 will be examined each year. If K-8 is treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0318, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECT

J.P. Thomas, University of Alabama in Birmingham, School of Dentistry, Dept. of Dental Research, *1919 7th Ave. S., Birmingham, Alabama* 35233 (N01DE52463 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0319, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECTS

L.F. Szwejda, State Dept. of Public Health, *3500 N. Logan St., Lansing, Michigan* 48914 (N01DE52466 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0320, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECT

A.J. Terrill, State Dept. of Health & Environmental Sciences, *State Laboratory Bldg., Helena, Montana* 59601 (N01DE52467 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0321, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECTS

S.R. Fishman, Virginia Commonwealth University, School of Dentistry, Dept. of Community Dentistry, *901 W. Franklin St., Richmond, Virginia* 23284 (N01DE52468 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explore. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0322, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECT

R.H. Schaefer, Independence Neighborhood Council, *600 W. Mechanic St., Independence, Missouri* 64050 (N01DE52469 (CONTRACT))

Establish and conduct a school-based caries prevention demonstration program; report data on the cost-effectiveness of the program; develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with a 0.2 percent solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Costs and staff time for implementing and conducting the project will be recorded.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0323, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECT

S.J. Silverstein, University of California, San Francisco Campus, School of Dentistry, Dept. of Prev Dentistry & Comm Health, *551 Parnassus Ave., San*

Francisco, California 94122 (N01DE52470 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $0

1.0324, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECT

L.A. Friedman, University of Texas, Health Science Center at Houston, Dental Branch, Dental Science Institute, *6515 Freeman, Houston, Texas* 77025 (N01DE52471 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $0

1.0325, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECT

R.H. Reger, State Dept. of Health, *4210 E. 11th Ave., Denver, Colorado* 80220 (N01DE52472 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with a 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $0

1.0326, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECT

G.D. Bissell, Research for Health in Erie County Inc., *462 Grider St., Buffalo, New York* 14215 (N01DE52473 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0327, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECTS

C. Sherman, Geauga County General Health District, *219 Main St., Chardon, Ohio* 44024 (N01DE52474 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explore. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0328, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECT

I.L. Dogon, Harvard University, Boston Campus, School of Dentistry, Dept. of Operative Dentistry, *188 Longwood Ave., Boston, Massachusetts* 02115 (N01DE52475 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school-based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2% solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three years after the Federal support has terminated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

1.0329, DIFFUSION OF PREVENTIVE HEALTH MEASURES TO SCHOOLS

J.B. Silversin, Harvard University, Boston Campus, School of Dentistry, Dept. of Dental Ecology, *188 Longwood Ave., Boston, Massachusetts* 02115 (R01 DE 05115-02)

This three-year study which commenced October 1, 1978 is designed to determine which factors discriminate between the adoption and nonadoption of primary preventive health measures in United States public schools. School-based self-applied fluoride programs have been selected as the prototype measure for study because of their ongoing rapid adoption within schools where an estimated 12 million children are currently participating in either fluoride rinse or tablet programs. The study design is based on specific hypotheses derived from classical diffusion of innovation theory and research concerning the diffusion of medical and educational innovations.

Through a series of mailed questionnaires to superintendents, principals, school health personnel, as well as site visits for in-depth analysis of the adoption process, data will be collected about who makes and influences decisions about health programs, aspects of the health measure itself that make it attractive to adopt, barriers and problems in implementing self-applied fluoride procedures including the extent of inappropriate or incorrect implementation; and an assessment of the extent to which schools are feasible sites for providing other health and medical services.

Discriminant function and regression analyses will be used to determine whether and to what extent the hypotheses proposed explain schools' decision whether or not to adopt self-applied fluoride rinse programs or other preventive measures.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $216,817

I. CARIES

1.0330, A COMMUNITY CARIES PREVENTION DEMONSTRATION PROGRAM, ISLAND OF GUAM

R. Louie, U.S. Dept. of Health & Human Services, *San Francisco, California* (Y01DE60020 (CONTRACT))

SALIENT RESULTS TO DATE: The program is running smoothly in the 12 schools for data collection and the 33 schools in the Island. The 7th grade has been added to the population for the second year. They now have a total of 13,479 children mouthrinsing.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$9,615

II. PERIODONTAL DISEASE

EPIDEMIOLOGY

2.0001, INTERNATIONAL WORKSHOP - RESEARCH IN PERIODONTAL DISEASE

B. Klavan, University of Illinois, Medical Center at Chicago, School of Dentistry, Dept. of Periodontics, *1853 W. Polk St., Chicago, Illinois* 60680 (R13 DE 04532-01)

The objectives of this international conference-workshop are: 1. Assemble at least 75 noted authorities from throughout the world in the area of periodontal research. 2. Review and evaluate the research of the last decade related to periodontal disease. 3. On the basis of that review and evaluation make the following determinations: a) Areas of research to be strengthened; b) New areas of research; c) New research methodology; d) Research priorities. 4. The updating of periodontal research knowledge and dissemination to faculties of the world's dental schools. 5. The development of an up-to-date bibliography on research in periodontal disease. 6. Production of a publication (250 copies) of the results of the conference-workshop for distribution to dental school libraries.

The above objectives will be achieved by the University of Illinois College of Dentistry hosting a conference-workshop under the direction of a steering committee, who given a model will plan and implement the methodology and time frame for achieving the objectives.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0002, A LONGITUDINAL AND CROSS SECTIONAL STUDY OF ORAL HEALTH IN HEALTHY MALE VETERANS

H.H. Chauncey, U.S. Veterans Admin., Dept. of Medicine & Surgery, Outpatient Clinic, *17 Court St., Boston, Massachusetts* 02108 (750-001-P)

One hundred and fifty-three subjects volunteered to participate in an investigation of salivary chloride levels, task thresholds for salt and sucrose, and food selection. They completed and returned a comprehensive food intake questionnaire designed to elicit use frequency of high salt and sugar food items and perceived salt and sugar use. A comprehenisve intake score was developed for each participant.

The results indicate relationships among certain of the variables examined; specifically a relationship between salt intake and age, salt intake and taste threshold, and between taste threshold and salivary chloride. Older subjects tested frequently mentioned a voluntary restriction of salt intake as a preventive health care practice.

If salivary composition and/or tast thresholds are to be used as markers for disease, studies of normal subjects are essential. Behavioral correlates of changes in salivary composition and changes in taste perception are being identified.

Two tests of masticatory function were done using age as a covariate. Subjects were divided into five dentition subgroups, according to the number of teeth present and the type of prosthetic replacement for missing teeth. As expected, natural dentition decreased and was replaced by a prosthesis as the subjects increased in age. However, within each subgroup, masticatory function, as measured by performance did not significantly alter with age.

A significantly difference did appear in the number of strokes used to prepare the test food for swallowing; and observation not related to dentition status or performance as measured by final particle size.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

ETIOLOGY - PLAQUE

2.0003, PLAQUE FORMATION BY ACTINOMYCES NAESLUNDII

C.H. Miller, Indiana University, Indiana University - Purdue University at Indianapolis, School of Medicine, Dept. of Microbiology, *1219 W. Michigan St., Indianapolis, Indiana* 46202 (R01 DE 03537-02)

Actinomyces naeslundii forms plaque and is an important agent in human root caries and periodontal disease. Plaque formation is a primary pathogenic property of those organisms which cause these oral diseases, and elimination of plaque formation by A. naeslundii will decrease or inhibit its pathogenicity. Although A. naeslundii has the potential to form plaque under a variety of nutritional conditions, essentially nothing is known about the specific attachment mechanisms involved. The objective of the proposed research is to define the mechanisms by which A. naeslundii forms plaque. The approaches to this objective are: 1. standardization of adherence and aggregation assays; 2. determine the ability of substances to induce adherence and aggregation; 3. analyze products released from enzymatic degradation of A. naeslundii plaque; 4. chemically analyze materials extracted from A. naeslundii plaque and test their ability to induce adherence and aggregation; 5. detect the presence of cell-surface polymer binding sites by enzymatic degradation studies. The long-term goal of the proposed research is to approach prevention of plaque-associated oral diseases. The specific information gained from this research will provide a logical basis for the clinical use of substances or techniques to reduce the incidence of root caries, periodontal disease and coronal caries. This will increase the capacity of the clinician for the delivery of dental health care.

BIBLIOGRAPHIC REFERENCES: Miller, C. H., C. J. Palenik, and K. E. Stamper. Properties of Actinomyces naeslundii plaque. Internat. Assoc. Dent. Res. Abst. no. 512, 1978, p. 202. Palenik, C. J., K. C. Park, and C. H. Miller. Effects of cocoa on polysaccharide formation and aggregation of Actinomyces naeslundii. Internat. Assoc. Dent. Res. Abst. no. 508, 1978, p. 201.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0004, INITIATORS AND MEDIATORS IN PERIODONTAL DISEASE

E.H. Montgomery, University of Texas, Health Science Center at Houston, Dental Branch, Dept. of Pharmacology, *6515 Freeman, Houston, Texas* 77025 (R01 DE 03743-07)

OBJECTIVE: To determine the means by which human plaque initiates and maintains a gingival inflammatory reaction. Molecular sieve chromatography of human plaque extracts has resulted in the crude separation of inflammation-inducing components as assessed by the topical application of these fractions to the gingiva of beagle dogs (a model which simulates periodontal disease). Attenuation of the gingival inflammation-inducing activity of these plaque fractions following in vitro treatment with inhibitors such as proteases and spleen extract indicates the presence of heat stable, protease sensitive inflammatory factors. This investigation is designed to further separate and purify the active inflammatory factors in plaque by additional chromatographic and electrophoretic techniques. Initial screening for inflammation-inducing activity will be accomplished with the rat paw edema model and by intradermal testing (dye leakage) in rabbits or guinea pigs. Confirmation of gingival inflammation-inducing activity will be evaluated by topical application to the dog gingiva model and measurement of the crevicular fluid response. Treatment of the active fractions with inhibitors prior to in vivo testing will provide additional information regarding their chemical composition. Active fractions also will be evaluated for biological activities including hyaluronidase, protease, kinin-forming and complement activating properties. Host mechanisms involved in the inflammatory response produced by purified plaque components will be studied. Initiating mechanisms will be studied by pretreatment of the animals with agents such as cobra venom factor and antilymphocytic serum. Mediating mechanisms will be investigated by measurement of levels of endogenous mediators (kallikrein, kinin, histamine, prostaglandins) in crevicular fluid and by systemic treatment of the animals with the antagonists of endogenous mediators. The inflammatory parameters measured after treatment will be compared to those in the untreated systems. These studies will provide necessary information for establishing the most effective means of preventing and/or treating periodontal disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$53,521

2.0005, MOLECULAR TAXONOMY OF POTENTIAL PERIODONTAL PATHOGENS

A.L. Coykendall, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Restorative Dentistry, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 04721-03)

We propose to clarify the taxonomic relationships of several periodontal bacteria by comparng the base sequences of their deoxyribonucleic acids

(DNA). DNA will be extracted from cells lysed by combinations of penicillin, lysozyme, and sodium lauryl sulfate. The molar ratio of guanine and cytosine in the total DNA bases will be determined by thermal denaturation. DNA base sequence similarities will be assessed by hybrid reassociation on membrane filters, and in solution through the use of single-strand specific nuclease(s). Organisms sharing 80% or more common sequences will be considered to be the same species. Below 50%, organisms will not be considered as members of the same species. Between 50 and 80%, other taxonomic criteria, such as phenotypic similarity and pathogenic similarity, will be considered in determining taxonomic position. We propose to study specific strains resembling Eikenella, Bacteroides, Capnocytophaga, and Fusobacterium.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $32,800

2.0006, ACQUISITION, TRANSMISSION AND LOCALIZATION OF HUMAN ORAL BACTERIA

J. van Houte, Forsyth Dental Center, Dept. of Oral Microbiology, *140 Fenway St., Boston, Massachusetts* 02115 (P01 DE 02847-110021)

For summary: see 1.0106.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $44,412

2.0007, CEMENTAL CARIES AS A DENTAL PROBLEM - MICROBIAL ECOLOGY AND ITS RELATION TO PATHOGENESIS

H.V. Jordan, Forsyth Dental Center, Dept. of Oral Microbiology, *140 Fenway St., Boston, Massachusetts* 02115 (P01 DE 02847-110022)

For summary: see 1.0013.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $66,618

2.0008, NATURE OF THE MICROBIOTA ASSOCIATED WITH PERIODONTAL DISEASES

S.S. Socransky, Forsyth Dental Center, Dept. of Oral Microbiology, *140 Fenway St., Boston, Massachusetts* 02115 (P01 DE 02847-110023)

The present investigation will elucidate the nature of the microbiota associated with destructive periodontal diseases of the young adult aged 20-35. Predominant organisms from such lesions and lesions of other destructive forms of disease will be tested for their pathogenic potential in gnotobiotic rats and hamsters. Organisms whose classification is uncertain will be extensively characterized; attempts will be made to develop functional classification schemes. If specific organisms appear to be associated with specific disease processes, efforts will be made to devise selective media for their isolation and enumeration.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $74,021

2.0009, SEROTYPING OF MICROBES FOR DIAGNOSIS OF PERIODONTITIS

G.E. Kenny, University of Washington, School of Medicine, Dept. of Pathobiology, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (P50 DE 02600-130035)

A great variety of organisms are associated with periodontal disease and, most important, the organisms are present in striking mixtures. The extent of the flora has been recognized only through recent advances in anaerobic technology. Although a great variety of organisms have been isolated, information concerning their taxonomic status is so limited that identification of the predominant organisms in the flora is an arduous task suitable only to research laboratories. Serological identification of the organisms is possible only for certain groups such as the serotypes of Streptococcus mutans.

Large advances have been made in antigenic analysis of microorganisms in the past 10 years. Methods are now available for conveniently comparing microorganisms, with the most important advances being in the ability to detect surface antigens and the ability to prepare monospecific antiserum to given components.

The overall objective of the project is to study the antigenic similarities and differences between oral microorganisms, with an ultimate view to preparation of specific serological reagents which can be used for serotyping.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $89,234

2.0010, PLAQUE MICROFLORA IN THE ETIOLOGY OF PERIODONTAL DISEASE

B.L. Williams, University of Washington, School of Dentistry, Dept. of Periodontics, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P50 DE 02600-130037)

Recent progress in the general field of periodontal research has revealed a multiplicity of disease entities having clinical manifestations previously considered as either juvenile or adult forms of periodontitis. Limited studies to date have delineated a variety of defects in the cellular and humoral control of polymorphonuclear leukocyte (PMN) chemotaxis and in the lymphocytic responsiveness among patients with periodontal disease. Current research efforts of the Periodontal Diseases Research Group are directed toward the further elucidation of the nature of such defects and their influence in the pathogenesis of various periodontal disease states.

The objective of the proposed microbiological research program is to characterize the subgingival microflora of patients and healthy individuals who have also been selected for study under the Clagett Project entitled 'Periodontal Diseases.' This collaborative effort represents a unique opportunity for an in depth periodontal microbiological study of individuals whose clinical and immunological status have been extensively characterized, combining current research approaches to microbial taxonomy with those of immunology.

Three groups of patients with either adult periodontitis, or juvenile periodontitis or the generalized rapidly progressive periodontitis with advanced bone loss, of approximately 20 patients each and age-related controls will be sampled at the rate of two per month. Predominant isolates will be defined taxonomically by the use of at least 60 physical and physiological traits. Numerical taxonomy programs will be used for the identification and classification of the most significant organisms recovered. DNA homology studies will be applied to achieve a more precise classification of selected groups of organisms. The similarity of microbial populations in the subjects studied will be analyzed with non-parametric statistical tests and conclusions formulated with respect to microbial populations and dysfunctions of the immune response.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$108,300

2.0011, ORAL MICROORGANISMS IN PERIODONTAL HEALTH AND DISEASE

M.A. Listgarten, University of Pennsylvania, School of Dental Medicine, Dept. of Periodontal Research, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (P50 DE 02623-120009)

The central theme of this proposal deals with the relationship of the periodontal flora to periodontal disease. It consists of 3 main approaches to investigating this subject, namely: 1. Clinical studies in humans to determine on a morphological basis what types of microorganisms precede clinically detectable disease or appear following the onset of detectable disease, and whether some of these bacteria can be utilized as marker organisms to prognosticate the onset of disease and the timing of suitably spaced preventive treatment visits. 2. Localization of specific bacteria by immuno-electron microscopy of bacterial plaque pellets, using horseradish peroxidase-labeled antibody as a marker. 3. Morphological studies of the interaction of selected periodontopathic microorganisms with the germ-free rat periodontium.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$134,312

2.0012, RELATIONSHIP OF SUBGINGIVAL MICROBIOTA TO THE ETIOLOGY OF DESTRUCTIVE PERIODONTAL DISEASES

S.S. Socransky, Forsyth Dental Center, Dept. of Microbiology, *140 Fenway St., Boston, Massachusetts* 02115 (P50 DE 04881-030002)

The relationship of microorganisms to the etiology of destructive periodontal disease has been established. The purpose of the present investigation is to determine which microorganisms are associated with various forms of destructive disease. As an essential first step, the consistency of the microbiota present in individual untreated sites of destruction will be monitored by darkfield microscopy and selective media techniques. The data derived should indicate whether microbial populations vary significantly over time in individual sites, and whether observed alterations (if any) correlate with changes in clinical status.

The predominant cultivable microbiota in individual sites demonstrating active destruction during clinical monitoring will be determined using comprehensive morphologic and biochemical characterization techniques. The effect of therapy (either mechanical and/or chemotherapeutic) on the composition of the microbiota will be determined. The patients will continue to be monitored longitudinally to determine the rate of recolonization of suspected pathogens. Concomitant monitoring of clinical status will also be carried out in order to reveal relationships of the microbiota to progress of disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$198,000

2.0013, THERAPY AND PREVENTION OF PERIODONTAL DISEASE (HUMAN)

R.J. Genco, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (P50 DE 04898-030003)

SPECIFIC AIMS: A. To determine if therapy of gingivitis can be better accomplished by use of antiplaque agents along with mechanical debridement and personal plaque control. B. To determine if therapy of periodontitis can be more efficiently achieved with the use of antibiotics in addition to the standard therapeutic regime of debridement, surgery and plaque control. C. To determine if the use of antimicrobial or antibiotic therapy will result in better treatment of juvenile periodontitis (periodontosis). D. To determine the changes in bacterial flora associated with successful therapy as carried out above in A to C. E. To determine the changes in host response after therapy carried out according to A to C above. Specific host response measurements will include lymphocyte and neutrophil functions, as well as serum immunoglobulins, complement, and serum modulating factors which influence neutrophil and/or lymphocyte function. F. To determine the effects of behavioral aspects of motivation for bacterial plaque control in the treatment and maintenance after treatment of patients with periodontal disease. To this end it is proposed: (1) to identify social, behavioral, and attitudinal factors related to patient cooperation and improvement in periodontal therapy. (2) To develop and evaluate a structured interview for use in selecting patients for periodontal therapy and in selecting communication strategies for instructing individual patients in preventing procedures. (3) To develop and evaluate instructional approaches which are appropriate to the concerns and cognitive skill levels of various patients. G. To evaluate the use of antiplaque agents in primary and secondary prevention of periodontal disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$124,224

2.0014, CLINICAL RESEARCH CENTER FOR PERIODONTAL DISEASE - MICROBIOLOGIC STUDIES

W.E. Moore, Virginia Commonwealth University, Graduate School, *901 W. Franklin St., Richmond, Virginia* 23219 (P50 DE 05139-020001)

This project of the Clinical Research Center for Periodontal Disease at Virginia Commonwealth University is conducted in collaboration with the Anaerobe Laboratory, Virginia Polytechnic Institute and State University. The goal of this project is to identify the bacteria associated with defined periodontal states. The present focus is the bacteriology of moderate periodontitis in adults, acute necrotizing ulcerative gingivitis, and juvenile periodontitis. Depending on rate of progress, other periodontal states will also be studied. Samples are obtained clinically, dispersed and inoculated under anaerobic conditions using the roll tube technic, at VCU, then transferred to the VPI & SU laboratory for definitive taxonomic study. To date, more than 200 different bacterial species have been found, many of which are previously undescribed.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$179,460

2.0015, MICROBIOLOGIC STUDIES OF THE HUMAN ORAL STREPTOCOCCI

B. Rosan, University of Pennsylvania, School of Dental Medicine, Dept. of Microbiology, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (R01 DE 03180-09)

The group H antigen has been found to be a glycerol teichoic acid found in most strains of Streptococcus sanguis tested. The antigenic determinant appears to be a beta 1,6 diglucosyl glucoside and thus is immunochemically distinct from the type specific b antigen which contains an alpha 1,6 diglucosyl glucoside as a determinant. Both these polymers are found in the cell walls of S. sanguis. The teichoic acid in the group antigen appears to represent only 15% of the weight of the antigen, the remainder appears to be a heteropolymer consisting of rhamnose, glucose and galactose. Purification of the cell wall teichoic acids on Sapharose yields two serologically active fractions: a small amount of relatively high molecular weight antigen containing lipid and giving a possible hemagglutination test with either anti-teichoic acid serum or group specific antiserum; a low molecular weight deacylated teichoic acid which does not hemagglutinate is the major serologically active component. Attempts to obtain large quantities of the group antigen using the spent medium as a starting material was unsuccessful because the amount of teichoic acid was only 0.2% of cell dry weight. This observation suggest the teichoic acids in S . sanguis may not be secreted as in other streptococci but merely results from autolysis of small number of cells. The teichoic acids found in the spent medium are both acylated and deacylated. Strains identified as S. mitis contain no glycerol teichoic acids either in membrane, wall or in the spent medium. No group antigen has yet been identified for these organisms using the standard antigen extraction method, e.g., phenol-water, Rantz and Randall, sonication and Lancefield. Attempts are being made to obtain and compare extracts obtained by enzymatic lysis of the cells to determine if a common backbone polymer is present in these organisms. If found, it may be possible to modify the polymer and make antibody against the backbone to use as a grouping antigen. The importance of grouping is seen in comparing adherence of oral streptococci to salivary coated hydroxyapatite, a model for plaque fromation. In these studies three distinct types of adherence to hydroxyapatite were detected. These interactions were correlated with the subtypes of S. sanguis.

BIBLIOGRAPHIC REFERENCES: Rosan, B. and B. Applebaum. 1979. A comparison of the extracellular teichoic acids of Streptococcus sanguis with the cell wall and cell membrane teichoic acids. Bacteriol. Proc. in Press. Rosan, B. and B. Appelbaum. 1979. An immunochemical study of Streptococcus sanguis and S. mitis. Proc. VII International Symposium on Streptococci and Streptococcal Diseases. In Press.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $95,140

2.0016, MICROBIAL COMPOSITION OF DEVELOPING DENTAL PLAQUE

S.S. Socransky, Forsyth Dental Center, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 03488-08)

The objective of this proposal is to study the changes in microbial composition of dental plaque during its longitudinal development and to determine some of the principles which may govern these changes. Plaque samples will be removed from supragingival, mid pocket and advancing front sites of patients with advanced periodontitis and supragingival and deep sites of patients with mild periodontitis. Samples will be taken at 6, 2 and 0 weeks before extensive debridement of the pocket site and at 2, 6, 12, 24 and 52 weeks after treatment. The samples will be removed by means of an oxygen free gas flushed syringe, and dispersed, diluted and plated using continuous anaerobic techniques. The predominant cultivable microbiota from each site at each time period will be extensively characterized as previously described. The results of the study should give insight into the nature of the microbial composition of subgingival plaque and the sequence of microbial recolonization after its removal.

Vibrios and 'corroding' bacteria have been found in high numbers in a number of pathological sites in the oral cavity including destructive periodontal disease. Many members of this group fail to fit current classification schemes. Approximately 100 isolates will be extensively characterized using biochemical tests, end product analysis, ultrastructural examination and determination of the moles percent G plus C in their isolated DNA. Data collected will be computer coded and analyzed by cluster analysis as well as by other means.

One of the principles which may govern the ecology of subgingival plaque is a dependence of certain groups of microorganisms on hydrogen evolution by other bacteria. Organisms will be sought in plaque which require hydrogen for growth. Attempts will be made to identify such organisms and enumerate both the hydrogen evolving and hydrogen utilizing organisms in dental plaques taken from sites exhibiting different disease states.

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U.S. Dept. of Health & Human
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National Inst. of Health,
National Inst. of Dental
Research $90,705

2.0017, ROLE OF DENTAL PLAQUE IN PERIODONTAL PATHOLOGY

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It is the purpose of the proposed research to trace and identify, by a combination of ultrastructural and immunohistochemical techniques, some of the components of bacterial plaque that are thought to be of importance in inducing and maintaining inflammatory reactions in the gingiva. The penetration of these substances through gingival epithelium and connective tissue and the sites of reaction with local defense mechanisms will be studied in order to contribute to a better understanding of the etiology and pathogenesis of periodontal disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $0

2.0018, SEROLOGY OF ORAL GRAM NEGATIVE ANAEROBES

S.J. Badger, Case Western Reserve University, School of Medicine, Dept. of Microbiology, *2109 Adelbert Rd., Cleveland, Ohio* 44106 (R01 DE 04422-03)

The microflora in deep periodontal pockets is predominantly gram negative rods. The antigenic relationships of these organisms is under investigation with emphasis on the vibrio-corroder group isolated at Forsyth Dental Clinic from patients with periodontal disease. The objective is to produce antisera which will identify these organisms on primary isolation and within tissues by use of indirect immunofluorescence (IFA).

Microagglutination studies have shown that Eikenella corrodens sps., Bacteroides corrodens sps., anaerobic vibrios and Campylobacter-like organisms do not cross react antigenically. Wall antigens are being isolated which will allow identification of six serogroups of Eikenella. Available sera are in use to identify the isolates from periodontitis patients and excised gingival tissues will be studied by IFA for possible colonization by vibrio-corroders.

High titer rat anti-Eikenella serum is in use to study the role of E. corrodens in the rabbit endocarditis model.

Transfer of genetic information by conjugation and transformation is being studied in the vibrio-corroder group.

The ultimate objective is to gain a better understanding of the incidence and pathogenic potential of the vibrio-corroder group of organisms in periodontal disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $0

2.0019, STUDIES OF THE PERIODONTAL FLORA

M.A. Listgarten, University of Pennsylvania, School of Dental Medicine, Dept. of Periodontics, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (R01 DE 04759-02)

This proposal is aimed in part at utilizing the diversity of ultrastructural features of bacterial cells to assist in their identification and taxonomic classification. This will be accomplished by comparing ultrastructural data with serological relatedness and biochemical characteristics for certain bacteria isolated from human mouths with and without periodontal lesions. Specific antibodies will be produced in rabbits against a selection of microorganisms which appear to predominate in periodontal lesions. These antibodies will be used to test the feasibility of localizing these bacteria in microbial smears obtained from the gingival sulcus or pocket area of human subjects or in pure cultures of bacterial isolates. The presence of circulating antibodies in the serum of human volunteers to the same selection of microorganisms will be tested by the indirect F.A. technique. Evidence will be sought for trends in labeling patterns which may be of value in the diagnosis and monitoring of clinical problems. The long term objective is to gain a better understanding of the microbial flora associated with periodontal disease, to learn how the flora and the periodontal lesion may vary in terms of the immune response of the host, and to develop practical means of identifying specific microbial components of the periodontal flora and circulating antibodies to these bacteria which may be of value for monitoring the severity and course of periodontal disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $171,276

2.0020, PERIODONTAL DISEASES - MICROBIOLOGICAL STUDIES

R.R. Ranney, Virginia Commonwealth University, School of Dentistry, Dept. of Periodontics, *901 W. Franklin St., Richmond, Virginia* 23284 (R01 DE 05054-01)

This proposal seeks to identify the bacteria present in human periodontal disease at the site of disease initiation and progression. It will further determine the quantity of each organism identified relative to the total number of organisms present, and assess the variability quantitatively at different sites, among individuals, and on repeated samples from the same site. Thus, baselines will be established for the reliability of single samples and the numbers of specific organisms present, related to total number of organisms present. The determinations will be made at the two ends of the spectrum of the most common form of periodontal disease, gingivitis-periodontitis; that is, gingivitis after starting from a healthy baseline, and severe periodontitis. Results from both groups will later be used for comparison to similar investigation in different severities of gingivitis-periodontitis and in other forms of periodontal disease. Results from study of the severe periodontitis group will complement on-going study of such a group relative to their immunologic status and responsiveness, and will aid in intelligent antigen selection for such studies. It is probable that previously undescribed organisms will be identified, and thus can be made available, descriptively and for purposes of comparison to isolates in other laboratories, to other investigators in similar or related studies.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $159,895

2.0021, CHARACTERISTICS OF DISEASE-RELATED CAPNOBACTERIA

S.C. Holt, University of Massachusetts, Amherst Campus, School of Natural Sciences & Mathematics, Dept. of Microbiology, *Amherst, Massachusetts* 01002 (R01 DE 05123-02)

Disease-related anaerobic gliding bacteria (Capnocytophaga) were isolated from the human oral cavity. Electron microscopic examination of thin-sections of chemically fixed cells revealed them to contain a periplasmic space of variable dimension and electron density. Electron microscopic and chemical localization and characterization of the hydrolytic enzyme alkaline phosphatase (APase) revealed it to be situated in the periplasm. The more virulent Capnocytophaga sputigena possessed twice as much APase activity than C. ochraceus and C. gingivalis. Localization of collagenase, elastase and other nucleotidases is in progress. High levels of branched chain fatty acids have been found in the capnobacteria; their significance and contribution to host tissue destruction is being evaluated; similar undertakings regarding secondary and tertiary amines has revealed large amounts of these compounds in several members of the genus Bacteroides. Studies involving the effects of these compounds on tissue culture cells is being planned. An extensive ultrastructural study on the surface structure of representative Capnocytophaga, Bacteroides and Eikenella has revealed large amounts of surface exopolymers of in vitro grown cells. These polymers not only join adjacent cells into a tight aggregate, but appear to attach the cells to the support surface. The contribution of these exopolymers to an in vivo existance is under examination.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $63,712

2.0022, IMMUNOIDENTIFICATION OF PERIODONTAL PLAQUE BACTERIA

A.J. Crowle, University of Colorado, Medical Center, School of Medicine, Dept. of Microbiology & Immunology, *4200 E. 9th Ave., Denver, Colorado* 80262 (R01 DE 05156-01)

The objectives of this project are to develop a rapid and specific immunochemical method for identification of human periodontal plaque bacteria. Identification will be by means of highly specific and possibly monospecific antisera developed and analyzed by means of two-dimensional electroimmunodiffusion (2-D EID). Specific immunochemical identification will be confirmed with the electron microscope in both pure cultures and directly in plaque. Correlations will be made between identifiable microorganisms present in a spectrum of periodontal diseases and in health.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $40,104

2.0023, GRAM-NEGATIVE BACTERIA OF DENTAL PLAQUES - PROPERTIES

E.R. Leadbetter, University of Connecticut, Storrs Campus, School of Liberal Arts & Sciences, Dept. of Biological Sci, *Storrs, Connecticut* 06268 (R01 DE 05348-01)

Gram-negative gliding bacteria associated with periodontal diseases will be fractionated and their exopolysaccharide, lipopolysaccharide, and peptidoglycan components purified, chemically characterized, and assessed for endotoxic activity.

A separate group of seemingly novel gram-negative bacteria also associated with periodontal diseases will be characterized in terms of morphological and physiological traits as an aid in the identification of them, and representative members of subgroups fractionated and assayed as above.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0024, COMPARATIVE PHYSIOLOGY OF LACTIC ACID BACTERIA AND OTHER ORAL MICROBES

J. London, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Microbiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00022-13 LMI B)

Xylitol, ribitol and d-arabitol can be utilized by certain strains of Lactobacillus casei and Streptococcus avium via a pathway unique to these microorganisms. The pentitols eventually enter the pathway of pentose metabolism and the ensuing heterofermentation of the sugar alcohols results in the production of lactate, acetate and ethanol. Regulation by glucose is not stringent and several of the enzymes involved in pentitol dissimilation continue to be synthesized while glucose is metabolized.

Gram negative isolates from subgingival plaque deposits have been characterized as cytophaga sp. These bacteria selectively colonize the root surfaces of teeth, softening and demineralizing the root structure in the process. The initial attachment of the organism to hydroxylapatite appear to be mediated by certain protein and lipid components of the cell's outer membrane.

BIBLIOGRAPHIC REFERENCES: Marucha, P.T., Keyes, P.H., Wittenberger, C.L., and London, J.: A rapid method for the identification and enumeration of oral Actinomyces. Infect. Immun. 21:786-791, 1978. Gibson, E.M., Chace, N.M., London, S.B., and London, J.: Transfer of plasmid-mediated antibiotic resistance from streptococci to lactobacilli. J. Bacteriol. 137:614-619, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$132,376

2.0025, HANDLING OF MICROBIAL STRAIN INFORMATION BY COMPUTERS

M.I. Krichevsky, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Microbial Systematics Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00044-09 ODIR)

Microbial strain data are being entered into a data bank which provides such services as: data on specific organisms and/or groups of organisms, a locator service for strains with special characteristics, identification of unknown isolates, cluster analysis definition of parameters of taxa, data management and report writing aids, aids in quality control, and communication of data via a common format. Files of primary data on a large number of microorganisms provide a resource for asking both ecological and epidemiological questions of interest in dental research. Programs are being developed and tested to enter, retrieve, and analyze the data in a variety of ways for epidemiological, diagnostic, taxonomic, ecological, etc. uses. The long term goal is to establish a worldwide data bank at a series of cooperating centers. The system originally developed for bacteria is now being expanded to include the algae, yeasts, molds and protozoa.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$57,033

2.0026, MICROBIOLOGICAL FEATURES OF CERVICO-RADICULAR PLAQUE IN HEALTHY AND DISEASED PERIODONTIUM

P.H. Keyes, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Microbiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00096-05 LMI)

Bacterial deposits, removed from the subgingival surfaces of teeth having healthy and diseased periodontal tissues, are being assessed by phase-contrast microscopy, fluorescent antibody techniques, and cultural methods. The bacterial complexes associated with disease differ markedly from those associated with health. Phase contrast microscopy reveals different complexes formed by stationary rods, cocci, spirochetes, motile rods, and amoebae. Populations of actinomyces also appear to differ. Some of the motile rods that have been isolated and studied appear to be strains of Cytophaga. Only a few of the highly prevalent spirochital populations have been isolated. Amoebae have been isolated, but maintained with difficulty. As determined by phase contrast microscopy, populations associated with disease can be shifted to those associated with health by antibacterial regimens that include: (1) debridement and decontamination of roots by the clinician, (2) the patient's daily use of certain inorganic salts and hydrogen peroxide to disperse and inactive root surface bacteria, (3) the occasional administration of tetracycline to suppress the microbiota not reliably controlled by the first two measures. Bleeding, suppuration, ulceration, hyperplasia, tooth mobility, halitosis, and resorption of bone abate as the microbiota associated with disease changes to that associated with health.

BIBLIOGRAPHIC REFERENCES: Marucha, P. T., Keyes, P. H., Wittenberger, C. L. and London, J. A rapid method for the identification and enumeration of oral Actinomyces. Infect. Immun. 21: 786-797. 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$115,703

2.0027, ALGORITHMS FOR MICROBIAL SYSTEMATICS

C.A. Walczak, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Microbial Systematics Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00250-02 ODIR)

A feature frequency analysis program has been written which tabulates features for groups of organisms and the uniqueness of each feature for each group. The uniqueness of a feature for organisms from a specific disease may be determined. Ranking the features by their mean deviations gives their ability to partition the groups most efficiently. We are developing an algorithm for displaying the level of redundancy of features to aid the microbiologist in choosing the 'best' set of features useful in identification by probabilities.

By appropriate redesign of numerical taxonomic programs, their versatility and cost effectiveness have been greatly enhanced. The similarity calculations may be used to develop group statistics using taxonomic and any other logic. This allows such direct comparisons as taxonomically derived groups with groups based on disease state from which isolated and, thus, detections of organisms associated with particular disease states.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$25,316

2.0028, STUDIES ON THE PROPERTIES OF ORAL ACTINOMYCETES

P.E. Kolenbrander, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00273-01)

The properties of oral actinomycetes which affect the potential of these bacteria to participate in cell-cell interactions with other oral microorganisms are under investigation. Many of the patterns of cell-cell interactions between the oral actinomycetes and oral streptococci have been elucidated. Results from a recent investigation using freshly isolated oral streptococci and actinomycetes not only confirmed earlier results with stock strains from national culture collections but also revealed additional patterns of coaggregation reactions. Currently, an extension of the type of investigation which described the coaggregation patterns between oral actinomycetes and streptococci is being conducted with oral gram-negative isolates. A great deal of specificity between certain Actinomyces israeli isolates and oral Cytophage isolates has been observed. It is expected that further investigation of bacterial cell-cell interactions will lead to better understanding of the natural mechanisms required to maintain these oral microorganisms in their ecological niche.

BIBLIOGRAPHIC REFERENCES: Cisar, J.O., Kolenbrander, P.E. and McIntire, F.C.: Specificity of coaggregation reactions between Actinomyces viscosus or Actinomyces naeslundii. Infect. Immun. 24:742-752, 1979. Costello, A.H., Cisar, J.O., Kolenbrander, P.E., and Gabriel, O.: Neuraminidase-dependent hemagglutination of human erythrocytes by human strains of Actinomyces viscosus and Actinomyces naeslundii Infect. Immun. In press. 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$52,382

2.0029, DENTAL STRESS TRANSIENT BACTEREMIAS FROM HUMANS WITH PERIODONTAL DISEASE ANALYZED BY QUANTITATIVE

AND QUALITATIVE ANAEROBIC CHAMBER METHODS

G.W. Carroll, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *3350 La Jolla Village Blvd., San Diego, California* 92161 (664-001-F)

Blood samples from 21 subjects with advanced periodontal disease were taken following a 30 minute rest period (unstressed condition), after chewing a meat strip, and after exodontia. 76.2% of the samples after exodontia were positive, all others were negative. Density levels of bacteria recovered ranged from 1-5 cells per 10 ml sample, with a mean of 2.3 cells.

The following isolates were recovered, the number indicates the number of subjects from which they were recovered.

Streptococcus MG-intermedius (2), Streptococcus sanguis II (3), Streptococcus sanguis III (1), Streptococcus mitis (2), Klebsiella ozaenae (1), Actinomyces viscosus (4), Propionibacterium acnes serotype 554 (1), Serotype 605 (1), Cross reacting 554-605 (5), Bacteroides corrodens (1), Bacteroides melaninogenicus (1), Fusobacterium nucleatum (2), Veillonella parvula (3), Peptococcus prevotii (3) unidentified anaerobic coccus (1).

The Fusobacterium nucleatum isolate is unique in that it is apparently the first extremely oxygen sensitive anaerobe to be isolated from a blood culture. This study gives additional support to the view that P. acnes is a normal member of gingival sulcus and obtains entrance to the bloodstream via tooth extractions. All pre-extraction controls samples were negative for P. acnes.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0030, MICROBIOTA OF THE PERIODONTAL ABSCESS

T.N. Sims, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-001-P)

Anaerobic techniques of isolation, processing and cultivation were used to determine the nature of the 'in situ' microbiota of the periodontal abscess. Several patients were examined on a longitudinal basis to determine the shift in pathogenetic organisms associated with improved clinical health. The results show that the periodontal abscess harbors a predominantly gram negative anaerobic microbiota, similar in some respects to chronic periodontitis. Strains of Bacteroids melanogenicus, Capnocytophga, B. corrodens, Fuscobacterium ssp. and other organisms described as vibrio corroding are found to predominate the acute periodontal condition.

Following successful periodontal procedures these organisms were significantly reduced. The heated sites were repopulated by a microbiota more compatible with periodontal health.

In addition to the cultural studies, analysis of the microbial samples with darkfield microscopy revealed numerous motile rod-shaped and spirochetal-shaped organisms. Following successful clinical therapy the number of these morphotypes were dramatically reduced. This suggests a good correlation between the treatment modality and the state of periodontal health.

The need to determine the progress and sequence of bacterial repopulation would be of great clinical significance in developing new forms of diagnosis and treatment. Future studies will attempt to elucidate these and other factors in the pathogenesis of the periodontal abscess.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0031, ANTIMICROBIAL SUSCEPTIBILITY TESTING OF ANAEROBES

V.L. Sutter, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Research Service, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-001-P)

The principal investigator, working with the National Committee for Clinical Laboratory Standards (NCCLS), has completed a 10 laboratory collaborative evaluation of a proposed reference dilution method for susceptibility testing of anaerobic bacteria. Analysis of results revealed minimal intra- and interlaboratory variation and allowed recommendation of the procedure. Results with 3 of the test strains were very consistent and allowed their recommendation as control strains. Five other strains were recommended as reference strains. The method and strains will be used in evaluating other procedures. The proposed method has been submitted to NCCLS for their consensus process and publication.

Studies are underway to evaluate a microdilution method for susceptibility testing of anaerobic bacteria and to determine the stability of antimicrobics in trays prepared and frozen for future use. If reliable, this method would provide a convenient means for rapid testing of bacteria from infections. The 8 strains from the NCCLS study are being used in this evaluation. To date, results of the tests are consistent with those obtained in the NCCLS study and even the least stable drugs in the penicillin class have remained stable for 6 months at -20 degrees C.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0032, PERIODONTAL DISEASE - BACTERIOLOGY AND ANTIMICROBIAL THERAPY

V.L. Sutter, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Research Service, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-002-P)

Studies are in progress to determine the most effective selective and nonselective media for isolation of bacteria from periodontal lesions and to evaluate rapid methods for their identification. The purpose of these studies is to expedite studies of the effect of antimicrobial therapy on the bacteria involved in periodontal disease. A study of 21 strains of Capnocythophaga, isolated from the gingival sulcus, periodontal lesions, blood, spinal fluid and transtracheal aspirates were characterized by conventional methods and a buffered single substrate (BSS) technique. Results showed that these organisms could be identified by the BSS technique with an appreciable savings of time and materials. Other groups of oral bacteria will be tested with this technique to further evaluate its usefulness.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0033, ANALYSIS OF THE SULCULAR MICROBIOTA IN DISEASE AND HEALTH

T.N. Sims, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-009-I)

Patients with moderate to severe periodontal disease will be divided into two groups. Each patient must have at least four periodontally diseased teeth and two unaffected teeth in a state of health. A diseased tooth will be selected to measure the effect of a low concentration of Stannous Fluoride. As controls, patients will have a similarly diseased tooth and an unaffected tooth. The similarly diseased tooth will serve as a comparison to chemical treatment of the other diseased tooth and the unaffected tooth will serve as comparison to both of the diseased teeth. A baseline analysis of subgingival microflora using dark field microscopy will be performed on all patients in both groups.

All bacterial samples will be taken by inserting a barbed broach with calcium alginate fibers to the apical extent of the involved pockets. Samples are then sonicated in a 1% gelatin solution and immediately dispersed on a glass slide. Following preparation these samples are then analyzed under a dark field microscope. Bacterial counts will be categorized according to morphological characteristics. In Group I patients, .4% Stannous Fluoride will be placed in an experimental pocket. In Group II patients, scaling and curettage will be performed on all teeth prior to placement of the .4% Stannous Fluoride in one of the experimental pockets. Sampling and analysis of the changes in the subgingival microflora will be done at 0 days, 2 days, 4 days, and 2 weeks.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0034, DENTAL PLAQUE AND THE PATHOGENESIS OF CHRONIC INFLAMMATORY PERIODONTAL DISEASE

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No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$8,372

2.0035, DIFFUSION PROCESSES IN THE ORAL ENVIRONMENT

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The aim of this research project is to develop a method to measure diffusion of metabolically important substances in dental plaque, pellicle and enamel. Additionally this system is being used to test the penetration into plaque and enamel of preventive agents such as fluoride.

A radioactive isotope of chemically inert xenon gas is allowed to dissolve into a thin layer of plaque of measured thickness. Measurement of the rate at which the xenon diffuses back out of the plaque enables the diffusion coefficient of xenon in plaque to be calculated. Xenon will fully penetrate a 100 micron layer of plaque within 13 seconds. Further modification of the technique permits measurement of the diffusion of sodium fluoride in plaque. The diffusion coefficient of NaF in plaque calculated from clearance curves is of the order of 5 x 10 to the minus 6th power sq. cm/s. It is concluded that plaque does not act as a significant barrier to the diffusion of small ions. The technique will be used to study the diffusion in plaque of larger ions and molecules, such as organic acids and sugars.

SUPPORTED BY

University of Glasgow	funds n.a.

2.0036, MECHANISM OF VIRULENCE OF ACTINOMYCES VISCOSIS T14V

D.C. Birdsell, State University System of Florida, University of Florida, School of Dentistry, Dept. of Basic Dental Sciences, *Gainesville, Florida* 32601 (R01 DE 04617-03)

The summary of differential virulence system of Actinomyces viscosus T14V and T14AV offers a unique opportunity to determine what macromolecular components of the resident plaque microbiota are operative in either immune or non-immune based mechanisms of periodonal pathology. The studies supported in this proposal involve purification of high molecular weight antigens from the cell surfaces of these organisms utilizing biological correlates of pathology to identify the important antigens. At the same time, studies are being carried out to examine the environmental conditions that influence the quantity of relative antigens produced by the cell and the conditions that result in release of the antigen into the surrounding environment. In addition, the antigens are being utilized to develop an experimental mouse model to evaluate the mechanisms involved in periodontal pathology.

BIBLIOGRAPHIC REFERENCES: King, G., D. Birdsell, and S. Thiems. 1978. Evidence for Prostoglandin-Stimulated Bone Resorption by Actinomyces viscosus T14V. J. Dent. Res. 57 (Special Issue A): 144 (Abstract No. 280). Powell, James T., Werner Fischlschweiger, and Dale C. Birdsell. 1978. Modification of Surface Composition of Actinomyces viscosus T14V and T14AV. Infect. Immun. 21: (in press).

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $55,218

2.0037, PHOSPHOLIPASE ACTIVITY OF PLAQUE MICROORGANISMS

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Studies are aimed at determining whether phospholipase A (PL-A) of microbial origin can influence the presence of prostaglandins (PG) in periodontal disease by providing PG precursors in the gingival crevice and periodontal pockets.

Phospholipase A produced by plaque microorganisms will be purified and characterized. Purified preparations will be used to demonstrate their ability to release PG precursors from gingival fragments in vitro and for their potential to produce histopathological changes in tooth supporting tissues after subgingival injections into experimental animals.

Microorganisms obtained from pockets of individuals with various periodontal syndromes will be screened to determine whether they can synthesize PG-like substances if provided with the proper precursors. This screening will be performed by following the conversion of 3H-arachidonate to substances that cochromatograph with known PG's.

Both PL-A and PG-like substances of bacterial origin will be assessed for their ability to promote fetal bone resorption in vitro.

BIBLIOGRAPHIC REFERENCES: Bulkacz, J. and Scott, D.F. 1978. Extracellular phospholipase A from Streptococcus mutans strain 6715. J. Dent. Res. 25:194. Bulkacz, J. and Scott, D.F. 1977. Phospholipase activity of Streptococcus mutans 6715. J. Dent. Res. 56: Special issue B, Abstract 0534.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $53,725

2.0038, VIRULENCE FACTORS OF GRAM NEGATIVE CORRODING BACTERIA

A.M. Slee, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Oral Diagnosis, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 04808-01A1)

The primary objective of the research proposed herein is the identification of the determinants of virulence (virulence factor(s)) of Gram negative corroding anaerobic/microaerophilic bacteria that have been implicated in periodontal disease. It is proposed to initially investigate the occurrence of virulence factors in strains of two Gram negative, corroding organisms, Eikenella corrodens and Bacteroides corrodens, both being isolated in significantly elevated numbers in patients diagnosed to have aggressive periodontal disease. Recent studies have demonstrated that certain microorganisms produce mediators which behave, in many but not all respects, like mediators (lymphokines) produced by sensitized lymphocytes. Such mediators have been implicated in a number of pathological reactions. Thus, the initial studies of this project will be directed towards the determination of whether selected strains of E. corrodens and B. corrodens produce and/or release lymphokine-line mediators. Preliminary data indicates that the spent culture fluids of these organisms possess both macrophage migration inhibition and chemotactic mediator activities. Studies will be undertaken to determine further if these microorganisms produce and release lymphokine-like mediators into their environment or whether such factors are components of the outer cell envelope. Filtrates of spent culture media and components of the cell envelope will be assessed using in vitro assays for the following mediator activities: chemotactic activity, migration inhibition for macrophages and neutrophiles, mitogenic activity and cytotoxic activity. It is proposed to isolate such lymphokine-like mediators using chromatographic techniques. Furthermore, to correlate production/release of such mediators it is proposed to demonstrate their in vivo production/release and to demonstrate that administration of purified preparations of such mediators when administered via injection into the gingival tissue of rats produce histological changes consistent with those noted in the infection with whole microorganisms. In addition, it is proposed to select for strains initially on the basis of colonial morphology which fail to produce lymphokine-like mediators and to determine if these strains can infect and produce a disease profile similar to that induced by known virulent progenitor strains.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $53,084

2.0039, PERIODONTAL DISEASE--ROLE OF SPIROCHETES

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Our goal is to elucidate the role of oral spirochetes in periodontal disease. Conditions for the isolation and propagation of these spirochetes must be established so that the basic biology of these bacteria can be studied. This will be necessary before infectivity studies can be undertaken.

SUPPORTED BY

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National Inst. of Health,
National Inst. of Dental
Research $37,666

2.0040, DNA HOMOLOGIES AMONG BACTERIA OF PERIODONTAL DISEASES

J.L. Johnson, Virginia Polytechnic Inst. & State University, School of Agricultural & Life Sciences, Anaerobic Bacteriology Laboratory, *Blacksburg, Virginia* 24061 (R01 DE 05218-01)

Basic to understanding the role of specific bacteria in the etiology of periodontal diseases is their accurate recognition and identification. Basic to the identification process is that the strains to be identified must be compared with strains that have been identified (data base). The success of any identification procedure or the evaluation of any (manual or computer automated) identification procedure is dependent upon a data base of accurately identified strains. A major objective of this project is to establish genetic relationships, by DNA homology experiments, among broad groups of bacteria that have been isolated from both normal oral cavities and from those with the various types of periodontal disease. The DNA results will provide the data base on which identification procedures can be evaluated.

The second major objective of the proposed study is to investigate the ecology of the oral microbiotota in terms of specific strains. Isolates that are identical can be so identified by DNA homology experiments. We will be able to establish if the flora of the oral cavity of an individual consists of strains that are unique to that individual. If this is so, we will be able to determine if organisms isolated from periodontal disease lesions are part of that individual's normal oral flora and will also be able to determine the effect of chemotherapy upon the resident strains.

The third major objective is to determine the distribution of plasmids among strains within the various DNA homology groups. The genetic relationships of these plasmids with each other will be determined by DNA homology. Phenotypic properties will be correlated with the presence of specific plasmids.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $88,917

2.0041, A GENETIC-BIOCHEMICAL ANALYSIS OF SPIROCHETE MOTILITY

N.W. Charon, West Virginia University, School of Medicine, Dept. of Microbiology, *Morgantown, West Virginia* 26506 (R23 DE 04645-02)

Spirochetes are a group of medically important bacteria which have been poorly studied. We do not understand some of the most fundamental aspects of nutrition, structure and function, and mechanisms of pathologenesis. One unique aspect of all spirochetes is rapid motility and distinct structure. As compared to other flagellated bacteria, where the flagella are external to the cell wall, spirochetes contain flagella-like structure (axial filaments) which are internal. That is, these filaments and the bacteria are ensheathed by a membrane. It is difficult to understand at this time how they propel themselves. We do not even know if these axial filaments play a role in motility.

We propose to use a genetic-structural and biochemical approach towards understanding how spirochetes move. We are using Leptospira as our model system, as these spirochetes are the easiest to grow in the laboratory. Our future plans include similar experiments on oral treponemes once the methodology has been developed. Our approach is to mutagenize Leptospira with nitrosoguanidine and ultraviolet light and isolate colonies which do not spread on agar. Presumably these bacteria will be motility mutants, as determined by darkfield microscopy. We have isolated a number of such mutants by this technique. Our next step is to analyze these mutants by electron microscopy and by chemical analysis of the mutant axial filaments. We have found that many of these motility mutants synthesize aberrant axial filaments as observed by electron microscopy. This is the first suggestive evidence that axial filaments play a role in spirochete motility. We are now purifying these filaments and comparing them morphologically and chemically to normal filaments. Our final step is to analyze whether motility revertants of these mutants regain normal axial filaments. The results would indicate whether the combined motility and aberrant axial filament phenotypes are the result of a pleotrophic mutant or multiple mutations.

BIBLIOGRAPHIC REFERENCES: Charon, N.W., A.M. Campbell, S.C. Stamm. 1979. Isolation of lambda transducing phage with the bio genes inserted between lambda genes P and Q. Genetics. Charon, N.W., S.A. Olenchock, M.J. Peach, III, T.D. Thedell, S.M. O'Brien, and P.C. Major. 1979. Direct culture and antibody screening for evidence of Leptospira in port grain terminals. Proceedings of the VII International Congress of Rural Medicine.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$26,410

2.0042, BIOSYNTHESIS OF SURFACE POLYMERS BY ORAL ACTINOMYCES

V.M. Reusch, University of Denver, School of Arts & Sciences, Dept. of Biological Science, *2115 S. University Blvd., Denver, Colorado* 80210 (R23 DE 05135-02)

The overall goal of this research is to contribute to the understanding of the biochemical mechanisms of the induction of periodontal disease in man. The biosynthesis of cell surface carbohydrate antigens will be studied in Actinomyces viscosus T14, a human oral bacterium that forms plaque and evokes periodontal disease in experimental animals. The major neutral sugars of the cell wall are rhamnose and 6-deoxytalose (DOT). The linkage between carbohydrate and peptidoglycan will be probed by hydrolytic procedures that are selective for phosphodiesters, and by overall chemical analysis. These studies will indicate the nature of nucleotide sugar substrates that are required for cell wall biosynthesis. The assembly of cell wall subunits will be studied in chemiclly treated whole cells.

If the DOT-containing antigen is essential in the pathogenicity of A. viscosus T14, the absence of DOT in mammalian tissues offers hope that agents, which could block either its synthesis or its incorporation into polymers by Actinomyces, would be innocuous to man and might be useful in suppressing the pathogenicity of Actinomyces in dental plaque. Accordingly, an understanding of the biosynthesis of the DOT-containing polymers should expedite the dicovery of such useful agents. Success in the endeavor might set a pattern of investigation which, through application to other oral pathogens, might contribute in a major way to the control of periodontal disease and caries.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$33,446

2.0043, BIOSYNTHETIC STUDY OF DENTAL PLAQUE POLYSACCHARIDES

J.F. Robyt, Iowa State University of Science & Technology, College of Humanities & Sciences, Dept. of Biochemistry & Biophysics, *Beardshear Hall, Ames, Iowa* 50010 (R01 DE 03578-08)

The application proposes the further purification of dextransucrase from Leuconostoc mesenteroides B-512 by hydrophobic and affinity chromatography. The purified enzyme will be used to study the nature of the groups binding dextran and glucose at the active site. The chemical structure of the acceptor products that results when low molecular weight oligosaccharides react with dextransucrase and 14C-sucrose will be studied using the layer chromatography and dextranase action. The two glucosyltransferases from Streptococcus mutans will be separated and their individual mechanism of action will be studied separately and together.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $52,461

2.0044, HOST BACTERIAL INTERACTIONS IN PERIODONTAL DISEASE

M.G. Newman, University of California, Los Angeles Campus, School of Dentistry, Dept. of Dentistry, *405 Hilgard Ave., Los Angeles, California* 90024 (R01 DE 04441-03)

The objective of this project is to study the nature of the host-bacterial interactions in the spectrum of periodontal health to periodontal disease with the ultimate goal of developing means for rapid identification of potentially pathogenic microorganisms. This project is aimed at providing fundamental lesions and in normal sulci from aged individuals with minimal periodontal disease. The predominant cultivable microbiota from the patients will be characterized by cultural techniques. Subsequent identification of these organisms in clinical material will employ immunologic techniques. The periodontopathic potential of prominant groups of microorganisms will also be assessed in experimental animals. Because host resistance factors influence periodontal health or disease humoral antibody responses to selected microorganisms will be studied.

Special attention will be focused on the Gram negative anaerobic rods which are numerically prominant in human dental plaque associated with alveolar bone destruction.

Such knowledge will be evaluated towards the development of practical means of prevention and control of periodontal disease.

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SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $94,720

2.0045, ROLE OF BACTERIAL PRODUCTS IN PERIODONTAL DISEASES

A.H. Nowotny, University of Pennsylvania, School of Dental Medicine, Dept. of Periodontics, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (R01 DE 04777-03)

The role of immune response in the development of periodontitis is the subject of this project. As an animal model for these studies, germ-free Sprague-Dawley rats are monoinfected with bacteria. The bacterial strains for this study are selected from those microorganisms which (a) were isolated from periodontitis patients and (b) which were already shown by others to induce periodontitis-like lesions in germ free rats. Measurements of the immune response to the monoinfecting microorganisms are carried out in longitudinal studies and correlation is sought between the immune response and the disease development.

BIBLIOGRAPHIC REFERENCES: D.A. Johnson, U.H. Behling, C.-H. Lai, M. Listgarten, S. Socransky and A. Nowotny. Role of Bacterial Products In Periodontitis II. Immune Response in Gnotobiotic Rats Monoinfected with Eikenella corrodens. Inf. & Immunity 19, 246-253, 1978. M. Listgarten, D.A. Johnson, A. Nowotny, A. Crawford and S. Socransky. Histopathology of Periodontal Disease in Gnotobiotic Rats Monoinfected with Eikenella corrodens. J. Perio. Res. 13, 134-148, 1978.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $107,058

2.0046, IMMUNOCHEMISTRY OF ORAL ACTINOMYCES SURFACE ANTIGENS

G.J. Revis, University of Colorado, Medical Center, School of Dentistry, Dept. of Oral Biology, *4200 E. 9th Ave., Denver, Colorado* 80220 (R23 DE 04290-03)

This investigation should contribute to an improved understanding of periodontal disease by providing immunochemical information about cell surface antigens which may act as virulence-associated factors for Actinomyces viscosus T14V. This organism is associated with plaque, root surface caries and the immunological sensitization of periodontal disease patients, and it also causes periodontal lesions in gnotobiotic rats. A mutant strain (T14AV) is avirulent for rodents and may lack virulence-associated antigen which is present in the virulent strain.

The fibrillar antigens are being purified from cell wall extracts. They will be characterized by: approximate molecular weight, sugar and amino acid composition, immunodominant groups, and effects on lymphocytes. Homogeneous proteins (lectins and mouse myeloma proteins) will be screened to detect binding activities for the fibrillar antigens and other cell surface antigens from A. viscosus T14V.

Special effort is being made for the preparation of more specific antisera to each fibrillar antigen. These antisera will be used to identify which antigen(s) may be responsible for coaggregation with Streptococcus sanguis 34, and to search for differences between virulent T14V and the avirulent mutant, T12AV.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0047, INVESTIGATION OF BACTERIAL ACID END-PRODUCTS FROM DENTAL PLAQUE

D.A. Geddes, Glasgow Dental Hospital & School, Dept. of Periodontology, *378 Sauchiehall St., Glasgow G2 3JZ, Scotland, United Kingdom*

Detailed investigation of bacterial acid end-products from dental plaque sampled from individual subjects after in-vivo incubation of sugars is being studied, using the new technique of isotachophoresis. This versatile electrophoretic separation technique permits rapid, direct and sensitive microquantitation of substances in an ionized form, their separation being a function of differences in their mobility. All major acidic end-products from plaque can be separated and identified in one analysis, thus avoiding the necessity of pooling plaque prior to analysis.

Preliminary studies indicate that formic acetic proprionic, butyric and lactic acids are all produced from in vivo metabolism of sucrose.

SUPPORTED BY

University of Glasgow	funds n.a.

2.0048, ACQUISITION, TRANSMISSION AND LOCALIZATION OF HUMAN ORAL BACTERIA

R.J. Gibbons, Forsyth Dental Center, Dept. of Oral Microbiology, *140 Fenway St., Boston, Massachusetts* 02115 (P01 DE 02847-110020)

The relative abilities of selected oral bacterial species to attach to teeth and to oral mucosal surfaces will be studied using both in vitro and in vivo approaches. The influence of salivary and serous components on bacterial attachment will be determined. Components studied will include those likely present in the acquired pellicle covering teeth as well as those free in oral fluids; special emphasis will be placed upon blood-group reactive mucins. Possible relationships between the composition of oral fluids as it influences bacterial attachment and susceptibility to infection will be determined. The influence of antibodies present in oral secretions on the adherence, colonization, antigenic composition and virulence of oral organisms will be assessed. The influence of various lectins, including those contained in certain foods, on the adherence and colonization of selected oral bacteria will be assessed. The roles of pili in colonization of Bacteroides melaninogenicus, and of motility for the colonization of selenomonas sputigena and Camplylobacter species will be evaluated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$88,823

2.0049, LIPIDS OF GRAM-POSITIVE RODS OF HUMAN DENTAL PLAQUE

B.H. Amdur, Forsyth Dental Center, Dept. of Periodontology, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 03529-05)

This project is attempting the isolation and identification of lipid constituents responsible for the tissue changes in animal gingivae equatable with human periodontal disease. It is also attempting to elucidate the involvement of the lipids of this group of bacteria isolated from human periodontal lesions (some assayed for virulence in gnotobiotic animal models) with plaque formation, by testing the effects on cell agglutination of both lipid active agents and of lipids isolated from specific cross agglutinating strains. The role of lipids in cell to hard surface adhesion is under investigation by modifying the surface lipids of the bacteria by selective enzyme action and by the employment of surfactants. Any interactions observed in the in vitro tests indicating therapeutic value will be tested in vivo in gnotobiotic rat models.

Besides the cellular fatty acid composition of the oral Gram-positive rods (determined by gas liquid chromatography) as an aid in classification, the intact lipids are also under survey. Both of these results are being correlated with studies on the same group of organisms by this and other laboratories including cell wall analyses, DNA base composition, metabolic reactions, antigenic relationships and other morphologic and biochemical characteristics, to establish the use of lipid 'fingerprint' as a taxonomic variable in this difficult-to-classify group of microorganisms.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0050, ADHERENCE OF PERIODONTAL DISEASE-ASSOCIATED BACTERIA

W.B. Clark, State University System of Florida, University of Florida, School of Dentistry, Dept. of Basic Dental Sciences/Immunology & Med Microbiology, *Gainesville, Florida* 32601 (R23 DE 05429-01)

The objective of this project is to study in depth the parameters which influence the adsorption of some prominent periodontal disease-associated bacteria to hydroxyapatite surfaces or epithelial cells under conditions which mimic the in vivo situation. Physical, chemical and environmental factors which may influence bacterial adsorption to surfaces will be investigated. The Langmuir adsorption model will be applied so that the comparative affinities and number of adsorption sites for the various strains can be obtained. The nature of the 'salivary receptor macromolecules' involved in the adherent interaction will be investigated. Particular emphasis will be placed on identification of cell surface 'receptor molecules' which interact with salivary components of epithelial cell surface receptors. Information on bacterial adsorption and bacterial cell 'receptor molecules' will be used in studies to follow these to attempt to develop practical means for preventing initial infection by periodontopathic bacteria in rodents and therefore lead to application for prevention of human periodontal disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$35,407

2.0051, MICROBIAL ANTIGENS ASSOCIATED WITH SPECIFIC ADHERENCE

J.O. Cisar, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Humoral Immunity Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00254-02 LMI)

Studies are continuing to examine molecular mechanisms by which species of oral actinomycetes adhere to other plaque bacteria and to mammalian cells. Lectin sites which are inhibited by lactose are associated with the surface fimbriae (i.e. pili) of many human strains of Actinomyces viscosus and A. naeslundii. These sites mediate coaggregation of the actinomycetes with certain oral streptococci and hemagglutination of the actinomycetes with neuraminidase-treated human erythrocytes. Thus, interactions of a lectin-carbohydrate type may contribute significantly to the distribution of certain bacteria within the oral cavity.

BIBLIOGRAPHIC REFERENCES: Cisar, J.O., and A.E. Vatter. 1979. Surface fibrils (Fimbriae) of Actinomyces viscosus T14V. Infect. Immun. 24:523-531. Cisar, J.O., P.E. Kolenbrander and F.C. McIntire. 1979. Specificity of coaggregation reactions between human oral streptococci and strains of Actinomyces viscosus or Actinomyces naeslundii. Infect. Immun. 24:742-752.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$70,454

2.0052, ENDOTOXINS AND ETIOLOGY OF PERIODONTITIS

J.F. Drummond, University of Kentucky, School of Dentistry, Dept. of Oral Pathology, *Limestone & Euclid, Lexington, Kentucky* 40506 (R01 DE 04083-03)

Much circumstantial evidence has been reported which links bacterial endotoxins to the etiology of inflammatory periodontal disease. However, precise data proving more than just a casual relationship between endotoxin and periodontal disease are unavailable. Before definitive correlations can be made between endotoxin and the periodontal disease process, certain key problems must be resolved. These problems include determining the ability of endotoxin to: (1) penetrate intact gingival sulcular epithelium, (2) induce chronic periodontal inflammation with associated bone loss, (3) activate the complement system in vivo (i.e., in gingival tissues).

A number of methods will be employed to study these problems in the beagle dog. 1. Gingival penetration will be examined by means of radiolabeling techniques. 2. The induction of inflammation by chronic application of endotoxin will be studied using classical histologic techniques, as well as clinical inspection and radiographic procedures. 3. The role of complement will be determined by assaying for the production of complement-derived chemotactic factors. Decomplementation of serum in vivo will further elucidate the importance of complement-endotoxin interaction.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

2.0053, ROLE OF PROSTAGLANDINS IN PERIODONTAL DISEASE

J.M. Goodson, Forsyth Dental Center, Pharmacology Section, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 04671-02)

By investigating the role of prostaglandins (PG) in periodontal disease, we have found that gingival PGE2 levels are elevated in diseased periodontal tissue to the extent that the observed bone resorption could be the result of a continued presence of this agent. Experiments are now planned to initiate investigation of the role of PG in the development of periodontal disease in gnotobiotic rats infected with organisms isolated from human periodontal disease.

The participation of PG in the disease mechanism will be tested by measuring gingival PG levels, excretion of urinary metabolites of PG and the effect of administrating drugs with PG-synthetase inhibitor effects. This will be the first animal test of these drugs in the treatment of periodontal disease and may be used for initial animal testing should these drugs exhibit therapeutic value in these animal models.

In addition, culture media supporting the growth of periodontal disease-associated organisms will be tested for bone resorption activity to identify etiologic substances elaborated by the organisms.

Drugs of the prostaglandin antagonist group will be further investigated for their abiliy to inhibit PG-mediated bone resorption.

The objective of these investigations is to determine the feasibility of treating certain forms of periodontal disease with drugs which interfere with the action of the prostaglandins and to test for causative chemical agents in cultures of periodontal disease organisms.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

2.0054, IMMUNOPATHOGENICITY OF HUMAN PERIODONTOSIS BACTERIA

J.R. Wetherell, Forsyth Dental Center, *140 Fenway St., Boston, Massachusetts* 02115 (R23 DE 04427-02)

Two strains of Gram negative anaerobic rods isolated from periodontosis patients have been shown to cause severe alveolar destruction as monocontaminants in gnotobiotic rats. The present investigation will attempt to measure the humoral and cellular immune response to the test organism in gnotobiotic rats using in vitro and in vivo measurements.

In a second series of experiments, gnotobiotic rats will be sensitized to the test organisms before or after implantation of viable organisms. The effect of sensitization on the immune response, the number of organisms per quadrant and the course of disease will be monitored using mirobiologic, immunologic and histologic techniques. Optimal chemotherapeutic agents will be sought in vitro to control the Capnocytophaga and Y4 organisms. The effect of such agents on the course of disease and microbial colonization will be monitored in gnotobiotic rats monoinfected by the suspected pathogens.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $2,839

2.0055, MAMMALIAN CELL CULTURE INHIBITORS IN DENTAL PLAQUE; ANTIBODIES TO PLAQUE ANTIGENS IN PERIODONTAL DISEASE

M. Levine, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *921 N.E. 13th St., Oklahoma City, Oklahoma* 73104 (635-001-P)

Precipitating serum antibodies to antigens from oral bacteria in dental plaque may be related to the severity of dental caries & periodontal disease & can be detected by immunodiffusion (ID) & immunoelectrophoresis (IEP). Toxic components from human dental plaque, detectable by their inhibiting the growth of mammalian cell cultures, may be important in the development of periodontal disease. Sera from 117 subjects were found to precipitate with culture filtrates of S mutans GS-5(S), A viscosus ATCC 19246 (A) & a soluble plaque extract (P). On IEP, precipitin arcs from A & S respectively migrated differently. Correspondingly migrating arcs were detected in P. Precipitins reacting to A & S were serologically non-identical but those to A & P were identical. Only 1 in 18 of subjects who reported brushing their teeth at least twice a day with infrequent bleeding from the gums reacted to S alone, whereas 1 in 4 of those reporting brushing less than twice a day or with frequent episodes of bleeding gums on brushing reacted to S alone (P less than 0.05). Subjects aged between 21 & 24 reacting to A or A and S had half the number of decayed/filled teeth compared to the rest (P less than 0.01). It is intended to purify the A,S & P antigens & further investigate their respective associations with oral hygiene, dental caries & gingivitis. A grant application is pending prior to further investigation of the toxic components of plaque. Presentation Abstract. Human serum precipitins to S mutans. M. Levine & V.K. Anderson J. Dent Res 58A 186 (1979).

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0056, MEMBRANE DYNAMICS IN THE SALIVARY EXOCRINE CELL

M.R. Robinovitch, University of Washington, School of Dentistry, Dept. of Oral Biology, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P50 DE 02600-130016)

For summary: see 1.0141.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$17,191

2.0057, ION TRANSPORT IN SALIVARY GLANDS - PERMEABILITY OF ORAL MUCOSA

E.L. Watson, University of Washington, School of Dentistry, Dept. of Oral Biology, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P50 DE 02600-130019)

For summary: see 1.0142.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$46,355

2.0058, MOLECULAR CELL BIOLOGY OF MEMBRANE FUSION

J.P. Segrest, University of Alabama in Birmingham, School of Dentistry, Dept. of Biochemistry/Microbiology/Pathology, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130030)

The interest of this laboratory is to study the physico-chemical properties of lipid-lipid and protein-lipid interactions as they relate to biological systems. Biological membranes are very complex and difficult to study. However, much can be learned about membranes through the systematic investigation of simpler, well-defined systems such as those proposed.

Membrane fusion will be investigated in two model systems: (1) fusion of liposomes (phospholipid bilayer vesicles) to the plasma membranes of cells in culture and (2) fusion of liposomes to other liposomes, specifically, small unilamellar-small unilamellar vesicle (SUV) interactions and small unilamellar-large unilamellar vesicle (LUV) interactions. The molecular properties of liposomes that are pertinent to an understanding of the process by which these liposomes appear to fuse to the surface membranes of living cells and thereby deliver their contents into the cell cytoplasm will be investigated. A long-term objective is to be able to use liposomes therapeutically for the treatment of cancer in vivo by the directed delivery of liposomally enclosed drugs to the cancer cytoplasms via fusion.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$32,058

2.0059, VITAMIN A IN BONES AND TEETH CALCIFICATION

J.M. Navia, University of Alabama in Birmingham, School of Dentistry, Dept. of Comparative Medicine, *1919 7th Ave. S., Birmingham, Alabama* 35233 (R01 DE 04862-02)

More than 50 years ago, vitamin A was recognized as an important nutritional factor in the calcification process of bones and teeth. Deficiency of vitamin A has been associated with severe malformations of bones characterized by an increase in their thickness and alterations of their normal structure and morphology. Teeth are also affected, particularly enamel and dentin, due to the atrophy and metaplasia of ameloblasts and odontoblasts deficient in vitamin A.

This proposal describes the approaches used to evaluate in a fully defined animal model system the biochemical effects of vitamin A deficiency in bone formation through the uptake of various radioactively labeled precursors and metabolites in a tissue culture system. Particular emphasis will be made in studying the effects of vitamin A in the metabolism of sulfated glycosaminoglycans of bones and teeth, as our previous work indicates these to be one of the matrix components affected by the nutritional deficiency. The effect of vitamin A deficiency on developing teeth will also be investigated with a view to evaluating their structure and composition and the susceptibility to dental caries.

The underlying hypothesis of this proposal is that vitamin A is essential to the calcification process of bones and teeth and that there is a critical time when this vitamin has to be available to allow normal calcification of mineralized tissues and to confer resistance to various disease stresses. Vitamin A has been found to be lacking in the diets of young children both abroad and in the U.S.A. In view of widespread deficiency of vitamin A in children who have not completed their dental and craniofacial development the biochemical role of vitamin A in calcification should be elucidated.

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SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $37,856

ETIOLOGY - MISCELLANEOUS ETIOLOGICAL FACTORS

2.0060, SCREENING FOR DIABETOGENIC VIRUSES

M. Dinowitz, Microbiological Associates Inc., *5221 River Rd., Bethesda, Maryland* 20016 (N01DE92420 (CONTRACT))

Provide services for a two-part screening procedure for detecting diabetogenic viruses. An estimated forty candidate diabetogenic viruses (provided by the Government) will be screened for their capacity to alter glucose homeostasis by infecting pancreatic islet cells of mice and rats. Results will be tabulated on data sheets and provided to the Government.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $125,450

2.0061, ROLE OF MAST CELL IN GINGIVAL AND PERIODONTAL LESIONS

M.L. Barnett, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Periodontics, *3435 Main St., Buffalo, New York* 14214 (R23 DE 04162-03)

The aim of this study is to elucidate the role of both the epithelial and connective tissue mast cell in the etiology and/or pathogenesis of selected human gingival and periodontal lesions, with particular emphasis on the sulcular lesion of chronic periodontal disease. The fine structure of mast cells associated with these lesions will be studied in human biopsies, using a technique which reliably preserves cytologic features including mast cell granules. Normal gingival specimens will provide baseline data. Information will be obtained regarding the distribution and morphology of mast cells; their cytologic features, including the presence and relative amounts of organelles involved in granule synthesis; signs of granule release; and the relationship of mast cells to other cell types and to regions of tissue damage. Staining of certain specimens with ruthenium red will allow for an accurate evaluation of mast cell degranulation. Special attention will be given to the intraepithelial mast cell. Interpretation of micrographs obtained will provide indirect information concerning mast cell function and activity in the specimens. More direct evidence regarding mast cell function will then be obtained by means of in vitro experiments using gingival explants. A system will be established for the study of mast cell degranulation in gingiva in vitro which can then be used to assess the effect of various substances, e.g., bacterial antigens. In addition, the possibility of gingival mast cells having a phagocytic role will be investigated in vitro by means of electron microscopy using an electron-opaque marker.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

2.0062, AN INTERDISCIPLINARY STUDY OF PERIODONTAL DISEASE, ETIOLOGIC AND TREATMENT FACTORS

C.L. Ricks, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *11201 Benton St., Loma Linda, California* 92357 (605-001-I)

This is a study of the interrelationships of some periodontal, prosthodontic, endodontic and restorative conditions and treatment modalities on oral health in animals; the information derived to be used as a basis for later experimentation and treatment in humans.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0063, ANTIGENS IN PERIODONTAL DISEASE IN MAN

L. Ivanyi, University of London, Inst. of Dental Surgery, Dept. of Oral Medicine, *Gray's Inn Rd., London WC1 8LD, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$27,228

ETIOLOGY - CONNECTIVE TISSUE STRUCTURE & FUNCTION

2.0064, EQUIPMENT LOAN FOR CONDUCT OF RESEARCH ON VERY LOW TEMPERATURE OPTICAL PHENOMENA DETECTABLE IN CONNECTIVE TISSUES

K.C. Hoerman, Loyola University of Chicago, Maywood Campus, School of Dentistry, Dept. of Preventive Dentistry & Community Health, *Maywood, Illinois* 60153 (N00014-79-C-0320)

There is a need to understand the aging process and nutritional aspects of connective tissue, tendon and collagen in dealing with the problems of dental care and dental surgery. Research in progress at Loyola University will provide such understanding. Equipment formerly used in Naval in-house studies in collaboration with Loyola is to be made available for this purpose.

A spectrophotofluorimeter, a PDP-12 computer, and ancillary equipment are to be used in studies of changes in quality and quantity of collagen correlated with normal aging, and with variations in nutrition in rats. Luminescent probing of fluorescence and phosphorescence from tendons cooled to about 2 degree Kelvin will provide the measures of the quality of the tendon structure.

SUPPORTED BY

U.S. Dept. of Defense, Navy, Office of Naval Research	$264,567

2.0065, FINE STRUCTURE OF EPITHELIAL ATTACHMENT, CEMENTUM AND PERIODONTAL LIGAMENT

O.P. Gupta, Howard University, Graduate School, *2400 6th St. N.W., Washington, District of Columbia* 20001 (S06 RR 08016-090009)

This project is part of a broader program (RR 08016-09) whose summary states: A renewal application is made for continued minority Biomedical support for the Biomedical Interdisciplinary Project at Howard University. It consists of individual research elements with biomedical relevance and requests for support of strong undergraduate and graduate student research participation. The subject areas of Botany, Chemistry, Dentistry, Immunology, Psychology and Zoology are represented among 19 research project elements organized by individual faculty members or collaboratively among faculty in two or more disciplines.

Support is requested for visiting scientists to serve as a part of a Seminar-Science Conference component designed to promote University-wide communication among faculty and student scientists at Howard.

Overall, a program is proposed which will ultimately increase the biomedical research potential at Howard and add to the pool of minorities trained and prepared to perform at a high level in biomedical research.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, Div. of Research Resources	funds n.a.

2.0066, PREPARE CULTURES OF EMBRYONIC CHICK LIMB CHONDROCYTES

A.I. Caplan, Case Western Reserve University, Case Inst. of Technology, Dept. of Biology, *2040 Adelbert Rd., Cleveland, Ohio* 44106 (N01DE72403 (CONTRACT))

The work called for in this contract will involve the preparation of radioistopically labeled proteoglycans from chick limb bud chondrocyte cultures. The proteoglycans will be labeled according to different pulse and pulse for further in-house experimentation. The chick limb bud cultures will be chondrocyte cultures can be obtained which represent different times in development. The methods used for the preparation of the cultured chondrocytes of the proteoglycans obtained from them are established and have been described in the literature.

II. PERIODONTAL DISEASE

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $23,964

2.0067, CONTROL OF COLLAGEN BIOSYNTHESIS AND DEGRADATION

P. Bornstein, University of Washington, School of Medicine, Dept. of Biochemistry, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (P50 DE 02600-130003)

Collagen synthesis and degradation must be carefully regulated in order to permit the development of a normally functioning organism and for successful homeostatic mechanisms. Indeed, morphogenetic and repair processes cannot tolerate even small deviation from an appropriate balance in these opposing processes without undesirable consequences. Collagen biogenesis and the dynamics of metabolism appropriate to a given tissue can be understood best by a precise biochemical definition of the steps involved and by localization of these steps to subcellular structures. It is therefore our aim to examine, in as detailed a manner as possible, (a) the biosynthesis and structure of procollagen; (b) the transcellular secretory pathway for this protein and the metabolic requirements for secretion; (c) the conversion of procollagen to collagen by limited proteolytic steps; (d) the manner in which these processes may be regulated by the extracellular environment; and (e) the role of disorders of biosynthesis in human disease. Insofar as possible, these studies will be performed in cell and organ cultures, systems which offer greater simplicity and flexibility for experimentation than the whole organism. An important purpose of this research is to identify points in the biosynthetic pathway at which physiological controls are exerted. It is expected that such information will be useful in the elucidation of disorders of connective tissue function in man and in the design of rational therapy of such disorders.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $175,095

2.0068, COLLAGEN BIOSYNTHESIS IN THE PERIODONTIUM

J. Rosenbloom, University of Pennsylvania, School of Dental Medicine, Dept. of Histology & Embryology, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (P50 DE 02623-120026)

The main objective of this research project is to apply recent advances in the biochemistry and molecular biology of collagen to problems related to diseases of the periodontium. Specifically we seek to (1) characterize the types of collagen and to determine the rates of collagen synthesis in normal and diseased gingiva, (2) elucidate control mechanisms in the biosynthesis of collagen, (3) evaluate the effects on collagen synthesis of factors generated during the inflammatory response. Normal gingiva and gingiva from patients with periodontal disease will be extracted with acetic acid and the residue digested with pepsin under controlled conditions. The solubilized collagen will be characterized by carboxymethylcellulose chromatography, polyacrylamide gel electrophoresis and analysis of cyanogen bromide peptides. Gingival biopsy fragments and gingival fibroblasts will be incubated with (14C) proline in vitro and collagen synthesis quantitated by (14C)hydroxyproline analysis and collagenase digestion.

We will attempt to define the level at which control of collagen synthesis is being exercised by extracting collagen mRNA from various cells and tissues and assaying it in a reticulocyte lysate system. We will test the possibility that isoaccepting species of tRNA may exercise control at the translation level. The fibroblasts found in the periodontium are exposed to numerous factors in the oral cavity which potentially can modify their physiologic response, particularly in inflamed tissues containing numerous blood cells. We plan to test a number of possible mediators derived from white blood cells on fibroblast proliferation and collagen synthesis.

Since connective tissue destruction is a cardinal feature of periodontal disease, there must be an aberration in the synthesis and/or degradation of collagen in the pathogenic process. Identification of the specific mechanisms involved must precede prevention and rational therapy.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $156,645

2.0069, COLLAGENASE IN THE PERIODONTIUM

P.J. Christner, University of Pennsylvania, School of Dental Medicine, Dept. of Histology & Embryology, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (P50 DE 02623-120027)

Periodontal disease is the major dental health problem of adult Americans. Because this disease involves the destruction of the connective tissue of the periodontium, a clear understanding of the mechanism of collagen destruction is necessary. Collagenase from polymorphonuclear leukocytes (PMNs), macrophages and fibroblasts will be isolated and purified to homogeneity and antisera will be raised to collagenases. The antisera will be purified to yield monospecific antibodies to the collagenases from each of the three sources. These antibodies will be used in a radioimmune competition assay to determine the cellular origin of the collagenase in the soft tissues of the human periodontium. The relative amount present and if possible the activity of each collagenase will be measured in both the normal and periodontally diseased gingiva and periodontal ligament. Immunofluorescent studies will also be carried out to localize the collagenases in the normal and diseased periodontium and to determine which cells are synthesizing the collagenase found there. Quantitative studies to determine the rate of synthesis, activation and secretion of collagenase in PMNs, macrophages and fibroblasts will be done. The effect of bacterial plaque, endotoxins and degradation products of collagen on these processes will also be measured.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $98,543

2.0070, ROLE OF MITOCHONDRIA IN THE MINERALIZATION PROCESS

I.M. Shapiro, University of Pennsylvania, School of Dental Medicine, Dept. of Biochemistry, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (P50 DE 02623-120030)

The purpose of this investigation is to study the role of mitochondria in the initiation of the mineralization process. We hypothesize that at the calcification front, intracellular events trigger mitochondrial calcium efflux. The released calcium is subsequently utilized for mineralization of the extracellular matrix. To test this hypothesis we propose to isolate mitochondria from proliferating and hypertrophic zones of the epiphyseal growth plate of the chick. These organelles will be characterized initially in terms of selected biochemical, morphological and functional criteria. We will then study the effects of oxygen tension and calcium loading on mitochondrial calcium release. Since changes in oxygen tension could lead to changes in the level of glycolytic intermediates and ATP, we will also ascertain whether these compounds modulate mitochondrial calcium efflux. The activity of mitochondrial phospholipase will be examined to determine whether calcium release is related to activation of this enzyme by calcium. Finally, we will investigate the hypothesis that specific carrier molecules are produced by these mitochondria to facilitate transcellular calcium transport.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $124,266

2.0071, METHODS FOR THE ULTRACYTOCHEMICAL DEMONSTRATION OF ENZYMES AND BIOMACROMOLECULES OF ORO- AND CRANIOFACIAL TISSUE

J.S. Hanker, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Oral Surgery, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130196)

The primary purpose of this research is the development of direct cytochemical techniques to study the cell biology, cell physiology and cellular pathology of craniofacial and orofacial tissues or tissues such as endocrine tissues, which affect their homeostasis. Because of the presence of diverse cell types, dense fibrous intercellular substances, and mineralization, indirect classical cell fractionation cytochemical techniques are only of very limited value. The direct techniques developed in this study are very precise and can be used at both the light and electron microscopic (EM) levels. Thus relatively large areas of tissue can be screened with the light microscope and ultracytochemical studies can be performed on the same tissue. The embedding and specimen selection techniques developed here permit EM studies on a cytochemical specimen after selection and study with the light microscope. Each of the new procedures will be perfected by application to a problem of particular interest to our laboratory. Thus the methods for phosphatases (including ATPase) will be used in studies of hard tissue formation and destruction. Methods for oxidoreductases including glycolytic dehydrogenases will be applied to study relationships, possible common origins and interactions of connective tissue cells of the periodontium such as the macrophage and fibroblast. Newly developed methods for demonstrating various glycomacromolecules will be also applied in this study. In addition they will be evaluated as nondistorting conductive coatings for SEM studies of biological specimens. New specific procedures for the light and electron microscopic demonstration of various collagens will be sought. Newer, more precise techniques and reagents for immunohistocytochemistry have been developed. These techniques, which afford greater specificity than classical histocytochemical techniques will also be applied to specific problems in craniofacial biology. Many of the methods developed in this program will be used to compare the metabolism of connective tissue cells harvested from the gingival sulcus of control patients with normal gingiva, nondiabetics with periodontitis and diabetics. The insoluble melanin-like polymers deposited by all of the cytochemical reactions described above gave products which displayed broad band fluorescence. Thus the cytochemically reacted cells may be sorted and counted on a fluorescence activated cell sorter.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$21,108

2.0072, ULTRACYTOCHEMICAL AND IMMUNOCYTOCHEMICAL STUDIES OF PERIPHERAL NERVES OF THE OROFACIAL REGION

J.S. Hanker, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Oral Surgery, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130197)

For summary: see 1.0183.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$10,554

2.0073, STRUCTURE OF CONNECTIVE TISSUE PROTEOGLYCANS

J.R. Baker, University of Alabama in Birmingham, School of Dentistry, Dept. of Biochemistry, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130029)

Some aspects of the structure of connective tissue proteoglycans are being investigated, mainly through studies on the chondroitin sulfate proteoglycan of bovine nasal cartilage. The 'link proteins,' which are components of cartilage proteoglycan aggregates and are believed to stabilize such associations, are the main subject of study. Methods of isolating and purifying the 'link proteins' have been established, and structural characterization is underway. Of primary interest is to determine the nature and importance of interactions between 'link proteins' and other proteoglycan aggregate components: hyaluronic acid and proteoglycan monomers. A specific immune procedure for identification and quantification of 'link proteins' has been developed, which will facilitate study of their occurrence in various connective tissues.

The major emphasis of the work during the next year will be on proteoglycan-link protein and proteoglycan-hyaluronic acid interactions. Interactions will be probed using specific antibodies and bifunctional reagents (i.e., various suberimidates) which can form stable cross links between interacting species.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$128,560

2.0074, CHEMISTRY AND PHYSIOLOGY OF PROTEOGLYCANS AND COLLAGEN OF CONNECTIVE TISSUES

D.D. Dziewiatkowski, University of Michigan, Ann Arbor Campus, School of Dentistry, *Ann Arbor, Michigan* 48104 (P50 DE 02731-130031)

The matrices of connective tissues, particularly cartilages, are under investigation as to (1) the composition of the proteoglycans in them and how the composition may change during growth and development, (2) the interactions of the proteoglycans with other components of the matrices, particularly hyaluronic acid, link protein, and collagen, (3) the degradation of the proteoglycans by endogenous proteases, i.e. cathepsin D. and (4) how the proteoglycans and their degradation products affect the biosynthesis of macromolecules by chondrocytes in culture.

A better understanding of the composition of the proteoglycans, their interactions, and metabolism is sought so as to gain insight of the function of these ubiquitous macromolecules in health and diseases.

To this end, techniques of biochemistry, physical chemistry, electron microscopy, immunology, and cell culture are employed.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$100,636

2.0075, LYSOSOMAL PROTEASES OF ORAL CONNECTIVE TISSUES

J.K. McDonald, Medical University of South Carolina, School of Medicine, Dept. of Biochemistry, *80 Barre St., Charleston, South Carolina* 29401 (R01 DE 04772-02)

The aim of this study is to identify the lysosomal proteinases contained within various oral connective tissus, and to characterize their substrate specificities on natural and artificial substrates. In particular, a new lysosomal enzyme detected in bovine dental pulp will be isolated and characterized and its demonstrated ability to hydrolyze, at acid pH, the prolyl bonds in collagen-related substrates will be fully investigated with reference to its potential contribution to collagen degradation. Fluorogenic substrates will be used in a sensitive fluorometric assay to assay for this enzyme (and other lysosomal enzymes) in human dental pulp, and in normal and inflamed periodontal tissues of human origin.

BIBLIOGRAPHIC REFERENCES: P.L. Sannes, J.K. McDonald, and S.S. Spicer. Dipeptidyl aminopeptidase II in rat peritoneal wash cells, Laboratory Investigation 37: 243-253, 1977.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$40,973

2.0076, STRUCTURAL STUDIES ON COLLAGEN

B.L. Trus, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Protein Chemistry Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00002-29 LB)

The primary goal of this project is an understanding of collagen structure from the molecular to the fibril level. Emphasis is presently on two main aspects of the general problem. 1) Computer enhancement and reconstruction of electron micrographs to reveal detail not obvious to the eye. 2) Three-dimensional computer models to study and illustrate structural features of collagen and molecular aggregates. Each of the above two approaches has led to the development of computer software that is being applied to other problems in protein structure and electron microscopy. A third aspect of this project, to relate amino acid sequence of collagen to higher level structure, has been inactive this year.

BIBLIOGRAPHIC REFERENCES: Piez, K. A. and Trus, B. L.: Sequence Regularities and Packing of Collagen Molecules. J. Mol. Biol. 122-419-432, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$65,278

2.0077, PROTEIN-CRYSTAL RELATIONSHIPS IN MINERALIZED TISSUES

J.D. Termine, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Molecular Structure Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00074-07 LBS)

The biochemical and biophysical properties of developing skeletal and dental tissue proteins are being studied by several techniques. Dentin, bone and enamel matrix proteins are also investigated as to their functional and structural influences on active mineralization in biological systems. Special emphasis is placed on phosphoprotein and glycoprotein biochemistry in these hard tissue matrix studies.

BIBLIOGRAPHIC REFERENCES: Peckauskas, R.A., Termine, J.D., and Pullman, I.: ESR studies on tooth phosphoproteins using manganese ions as probes. Arch. Biochem. Biophys. 193: 186-190, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$139,874

2.0078, STRUCTURE AND BIOSYNTHESIS OF PROTEOGLYCANS

V.C. Hascall, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Proteoglycan Chemistry Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00134-05 LB)

The purpose of the project is to study the chemical and physical properties of proteoglycans and their biosynthesis. Topics of present interest include: 1) chemistry of proteoglycans isolated from the Swarm rat chondrosarcoma, 2) mechanisms of proteoglycan aggregation and interaction with hyaluronic acid, 3) biosynthesis of the protein core of proteoglycans, the link proteins, and hyaluronic acid by chondrocyte cultures, 4) relationship between proteoglycan structure and extracellular matrix organization using chick limb bud chondrocyte cultures, 5) characteristics and biosynthesis of proteoglycans in corneal stroma.

BIBLIOGRAPHIC REFERENCES: Faltz, L. L., Reddi, A. H., Hascall, G. K., Martin, D., Pita, J. C., and Hascall, V. C.: Characteristics of proteoglycans extracted from the Swarm rat chondrosarcoma with associative solvents. J. Biol. Chem. 254:1375-1380, 1979. Oegma, T. R., Hascall, V. C., and Eisenstein, R.: Characterization of bovine aorta proteoglycan extracted with guanidine hydrochloride in the presence of protease inhibitors. J. Biol. Chem. 254:1312-1318, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$320,198

2.0079, BIOPHYSICAL STUDIES ON THE STRUCTURE OF CONNECTIVE TISSUE

D.A. Torchia, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Protein Chemistry Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00157-05 LB)

The purpose of this project is to investigate the molecular structure of fibrous proteins and of proteoglycans and to study phosphorus chemistry in connective tissues. The structural information obtained will be correlated with function. Areas of present interest are 1) Structure of collagen and elastin. 13C and 2H magnetic resonance techniques are being used to study the structure and interactions in collagen and elastin fibers. 2) Proteoglycan structure. 13C magnetic resonance is also being used to study the molecular mobility of the polysaccharide and protein chains in the chick limb bud proteoglycan monomer. 3) Phosphorus chemistry in connective tissue. Magic angle spinning 31P magnetic resonance is being used to probe the structure of the phosphorus moieties in connective tissue. 4) 13C magnetic resonance is being used to study the extent and mechanism of hemoglobin S gelation in cell-free preparations and in erythrocytes. For these studies, magnetic resonance spectrometers have been assembled which give 2H, 13C, and 31P spectra of solids. High power decoupling, cross-polarization, magic angle spinning, and solid echo experiments are all performed.

BIBLIOGRAPHIC REFERENCES: J. W. H. Sutherland, W. Egan, A. N. Schechter and D. A. Torchia: Carbon-13-proton nuclear magnetic double resonance study of deoxyhemoglobin S gelation. Biochemistry. 18:1797, 1979. L. W. Jelinski and D. A. Torchia: 13C/1H High power double magnetic resonance investigation of collagen backbone motion in fibrils and in solution. J. Mol. Biol. 132, 1979. in press.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$103,514

2.0080, CONNECTIVE TISSUE - FORMATION AND STRUCTURE

R.A. Gelman, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Protein Chemistry Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00215-03 LB)

It is the long range purpose of this project to study interactions and relationships between connective tissue macromolecules as a way to understand connective tissue formation and structure. The topics of present interest are: 1) The mechanism of collagen fibril formation in vitro. 2) High resolution electron microscopy of fibrils and early aggregates in collagen assembly. 3) Quasielastic light scattering. 4) The effect of noncollagenous molecules on collagen assembly in vitro. We have developed a reproducible in vitro assembly system and shown that collagen fibril formation is a multistep process. After an early initiation step that is not understood, linear assembly of thin filaments dominates, followed by lateral association of the filaments to form native collagen fibrils.

BIBLIOGRAPHIC REFERENCES: Gelman, R. A., Williams, B. R. and Piez, K. A.: Collagen fibril formation. Evidence for a multistep process. J. Biol. Chem. 254:180-186, 1979. Gelman, R. A., and Nossal, R.: Laser light scattering from mechanically excited gels. Macromolecules. 12:311-316, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$154,006

2.0081, BIOMECHANICS OF TOOTH SUPPORT

D.C. Picton, University of London, University College Hospital Medical School, *University St., London WC1E 6JJ, England, United Kingdom*

The objective of the project is to elucidate the mechanisms by which transient external loads are dissipated within the periodontal ligament and the surrounding bone. The roles of the different components of the periodontal ligament in Macaque monkeys are being clarified by drugs which affect the vascular and connective tissue elements.

SUPPORTED BY

(No Supporting Organization Reported)	funds n.a.

2.0082, AN AUTORADIOGRAPHIC AND E-M STUDY OF THE PERIODONTAL LIGAMENT FOLLOWING CHANGES IN ITS ERUPTIVE AND FUNCTIONAL STATE

B.K. Berkovitz, University of Bristol, Dept. of Anatomy, *Bristol BS8 1TH, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$23,370

2.0083, COLLAGEN FIBER CRIMPING IN THE PERIODONTAL MEMBRANE AN ITS POTENTIAL ROLE IN TOOTH ERUPTION, SUPPORT AND MOVEMENT

A.J. Darling, University of Bristol, Dept. of Dental Medicine, *Bristol BS8 1TH, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$16,019

PATHOLOGY - INFLAMMATORY RESPONSE

2.0084, MODIFICATION OF PERMEABILITY OF THE GINGIVAL CREVICE

M.C. Alfano, Fairleigh Dickinson University, Teaneck Hackensack Campus, School of Dentistry, Dept. of Periodontics & Oral Medicine, *Teaneck, New Jersey* 07666 (R01 DE 04480-03)

The penetration of toxic antigenic or enzymatic irritants from the subgingival plaque into the tissues of the gingival sulcus represents one of the most fundamental events in the initiation of inflammatory periodontal disease. Thus, the ability of the epithelium which lines the gingival sulcus to act as an effective barrier is an important mechanism of host defense. The purpose of this investigation is to evaluate mechanisms by which to improve the barrier function of sulcular epithelium.

Current studies focus on the relationship between dynamic measurements of sulcular permeability in various states of gingival inflammation and the ultrastructural correlates of barrier function. reproducible microperfusion system has been developed for the quantitative assessment of sulcular barrier function. This technique will be utilized in the systematic study of the effects of barrier active agents on gingival permeability.

BIBLIOGRAPHIC REFERENCES: 'Quantitative determination of sulcular permeability in the Beagle dog' M.C. Alfano, D. Fine and C.W. Masi. J. Dent. Res. (Special Issue A) 57:139 (Abst. No. 260) 1978. 'Characterization of oral mucosal permeability' G. Borzemsky, M.C. Alfano and T.S. Freund. J. Dent. Res. (Special Issue A) 57:222 (Abst. No. 590), 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0085, THE FUNCTIONAL PROPERTIES OF THE GINGIVAL INFILTRATE IN PATIENTS WITH PERIODONTAL DISEASE

D.M. Walker, University of Wales, Welsh National School of Medicine, Dept. of Oral Medicine & Oral Pathology, *Heath Park, Cardiff CF1 1XP, Wales, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$7,759

2.0086, STUDIES ON HUMAN PAROTID PROTEINS

P.J. Keller, University of Washington, School of Dentistry, Dept. of Oral Biology, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P50 DE 02600-130009)

For summary: see 1.0140.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$8,334

2.0087, CHEMOTAXIS - ITS ROLE IN PERIODONTAL DISEASE

L.C. Altman, University of Washington, School of Medicine, Dept. of Medicine, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (P50 DE 02600-130030)

Several lines of evidence have suggested a role for phagocytic cells in periodontal disease. Histologically, polymorphonuclear leukocytes (PMNs) are very prominent, especially in the early periodontal lesion; while more chronic lesions are infiltrated by mononuclear leukocytes (MNs). For this reason the possibility of PMN and/or MN-mediated tissue damage must be considered. However, the finding of an early onset of severe periodontal disease in certain patients with inadequate numbers of PMNs or MNs or impaired function of PMNs or MNs appears to implicate a protective role for these cell types. Particularly prominent among the phagocyte dysfunction syndromes associated with periodontal disease is disorder of chemotaxis. The proposed studies employ in vitro assays of PMN and MN chemotaxis to evaluate the potential role of directed migration of these cells in periodontal disease. Areas of major interest include (1) a survey of patients with unusual degrees or early onset of periodontal disease and patients with marked susceptibility to infection for defects in PMN chemotaxis; particular emphasis will be placed on patients with idiopathic juvenile periodontosis (IJP), and (2) the isolation and characterization of chemotactic factors that might be operative in periodontal tissues. Factors produced by bacteria associated with periodontal disease and factors derived from the host, such as complement-related products, will be considered. Attempts to identify these types of chemotactic factors in saliva and sulcular fluid will be made. Studies of salivary peroxidase in patients with IJP will also be initiated. It is hoped that this multi-faceted approach will advance our current understanding of the possible role of phagocytes and other oral host defenses in periodontal disease.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $62,712

2.0088, INTERACTIONS OF ORAL MICROORGANISMS AND POLYMORPHONUCLEAR LEUKOCYTES

W.P. McArthur, University of Pennsylvania, School of Dental Medicine, Dept. of Pathology, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (P50 DE 02623-120023)

Plaque and inflammatory cells have both been implicated in the interaction and perpetuation of periodontal disease. Polymorphonuclear leukocytes (PMNs) are the predominant inflammatory cells in contact with plaque deposits in the gingival sulcus. The objective is to examine the interactions of PMNs with plaque-derived microbial isolates. By understanding these interactions in vitro it is felt that clues will be obtained as to the inflammatory mechanisms involved in the disease. The specific aims are: 1. characterization of the in vitro PMN response to selected Gram-negative plaque-periodontopathogens; 2. examination of the effect of Actinomyces viscosus T14 products and constituents on human PMNs; 3. examination of the modulating effects of serum components on the interactions of plaque-derived bacteria and their products and constituents with PMNs. From such experiments we expect to define more completely the role of PMNs in periodontal and other inflammatory diseases as well as acquire a better understanding of the pathogenic potential of periodontal pathogens.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $80,121

2.0089, THROMBIN-PLATELET INTERACTIONS

G.C. White, University of North Carolina, Chapel Hill Campus, School of Dentistry, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130168)

The initial event in the healing of a vascular injury involves the formation of an aggregate of platelets referred to as the 'platelet plug'. Thrombin is a potent activator of blood platelets causing them to aggregate and release intracellular materials. This investigation proposes to examine the structural features of thrombin important in this reaction, to determine the identity of the thrombin receptor protein(s) on the platelet surface, and to identify and isolate substrate(s) for thrombin on the platelet surface.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $68,621

2.0090, CLINICAL RESEARCH CENTER FOR PERIODONTAL DISEASE - PMN FUNCTION STUDIES

R.A. Carchman, Virginia Commonwealth University, School of Basic Sciences & Graduate Studies, Dept. of Pharmacology, *901 W. Franklin St., Richmond, Virginia* 23284 (P50 DE 05139-020003)

This project has confirmed previous reports of deficient pmn chemotaxis in juvenile periodontitis. Attempts at determining the metabolic basis for the functional inadequacy have begun. Studies of calcium flux and cyclic nucleotide metabolism have proven inconclusive because of the difficulties in adapting these assays to human pmn, thus far. Attempts will continue, to determine if cyclic nucleotide metabolism is related to the chemotactic defect. We will also begin to try in vitro correction of the defect pharmacologically. Also, based on previous work and experience with synthetic chemotactic peptides, presence of peptides with chemotactic activities as products or components of oral bacteria has been started. Preliminary screenings indicate several bacteria isolated from periodontal pockets compete with chemotactic peptides for receptor sites on PMN. Scientific Classification Code: 20312

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $131,150

2.0091, HUMORAL AND CELLULAR MEDIATORS OF INFLAMMATION

R. Snyderman, Duke University, School of Medicine, Dept. of Medicine, *Box 3711*, *Durham*, *North Carolina* 27710 (R01 DE 03738-07)

This research is drected toward understanding the mechanisms by which the immune system initiates and controls inflammatory responses. Specifically, we will define the biochemical mechanism involved in the chemotaxis of leukocytes such as polymorphonuclear leucocytes, monocytes and macrophages. We will characterize the chemotactic factor receptors on leukocytes and see if abnormalities of such receptors are associated with inflammatory diseases such as periodontosis. We have recently demonstrated that transmethylation reactions mediated by S-adenosyl methionine are required for directed movement by human monocytes, guinea pig macrophages and guinea pig granulocytes. Phagocytosis, on the other hand, has far less stringent requirements for methylation indicating that chemotaxis and phagocytosis have different metabolic requirements. We have also shown that phospholipid methylation by leukocytes is altered upon their exposure to chemotactic factors. Production of phosphatidylcholine from phosphatidylethanolamine is inhibited in guinea pig macrophages by up to 70% following incubation with chemotactic factors. Changes in phospholipid composition following the binding of chemotactic factors may produce biophysical alterations in the membrane which are necessary for polarized cellular motility. We now seek to determine how chemotactic factors inhibit phospholipid methylation and exactly what role alterations in cellular phospholipid composition play in chemotaxis. In studies concerning the mechanisms of host resistance to endotoxin, it was found that in normal mice, 'native' endotoxin markedly suppresses the magnitude of intraperitoneal inflammatory responses to other inflammatory agents, whereas in 'nonresponder' C3H/HeJ mice, endotoxin does not suppress inflammation. The polysaccharide moiety of the endotoxin molecule is required for the suppressive effects. The mechanism by which endotoxin suppresses inflammation in normal mice is being investigated. In sum, the studies described here will elucidate biochemical mechanisms of inflammation and attempt to characterize the factors which govern the effectiveness and intensity of inflammatory reactions.

BIBLIOGRAPHIC REFERENCES: Snyderman, R., Meadows, L., Holder, W., and Wells, S. Abnormal Monocyte Chemotaxis in Patients with Breast Cancer: Evidence for a Tumor Mediated Effect. J. Nat. Cancer Inst. 60(4):737-740, 1978. Levy, S.B., Pinnell, S.R., Meadows, L., Snyderman, R. and Ward, F.E. Hereditary C2 Deficiency Associated with Cutaneous Lupus Erythematosus: Clinical, Laboratory and Genetic Studies, Archives of Dermatology 115:37-61, 1979.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $112,891

2.0092, BLOOD VESSEL RESPONSE IN PERIODONTAL DISEASE

J.M. Hock, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Periodontics, *Farmington Ave.*, *Farmington*, *Connecticut* 06032 (R01 DE 05188-01)

Increased knowledge of vascular function during chronic periodontal disease is likely to add to the knowledge of the disease process and of the prognosis for tissue recovery. The effect on bone metabolism of the vascular changes known to occur during chronic inflammation of the periodontium has not been investigated.

The objective of this research is to determine the role of blood vessels in alveolar bone resorption in dogs. Using an implanted minipump, a localized area of bone will be exposed to continuous infusions of low concentrations of mediators of either vascularization or resorption.

The vascular response associated with bone resorption will be measured as follows: vascular surface area and volume as determined by stereologic morphometry of 1 micron thick histologic sections; vessel type and numbers found as determined by stereologic morphometry and electron microscopy; sites of vessel growth as determined with autoradiography. Morphologic characteristics will be assessed using cleared, perfused tissue specimens.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $73,402

2.0093, LIGHT AND ELECTRON MICROSCOPY OF ORAL VASCULATURE IN DIABETES MELLITUS

T. Sist, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *3495 Bailey Ave., Buffalo, New York* 14215 (528-002-I)

This study proposes to investigate the light and electron microscopic features of vasculature from the oral mucosa of diabetic and non-diabetic patients. The tissue will be removed at the time of surgery for other purposes and will consist of attached gingiva taken during extraction procedures or periodontal surgery. The material will be collected from ten (10) control patients and ten (10) diabetic patients. Changes in vessel architecture, especially thickening and reduplication of the basement membrane will be noted and correlated with the clinical history of each patient. To date, five diabetic cases have been collected and light and electron microscopy has been performed.

SUPPORTED BY

U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

2.0094, PERIODONTAL DISEASES (HUMAN, NON-HUMAN PRIMATES, DOGS)

J. Clagett, University of Washington, School of Dentistry, Dept. of Periodontics, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P50 DE 02600-130014)

Periodontal disease is the most common cause of tooth loss in the adult human and is therefore a massive public health problem. It is generally agreed that our best opportunity for solution of the problem lies in research aimed at prevention. One important aspect of this research is investigation of the response of the host's tissues to the etiologic agent(s) responsible for the disease. In its earliest stages, the disease is characterized by an acute inflammatory response, an accumulation of lymphoid cells, and loss of a major portion of the collagen present in the marginal gingiva. Subsequently, plasma cells become the predominant cells present, and fibrosis of the soft connective tissues becomes apparent. Immunopathologic and other destructive inflammatory mechanisms appear to play a major role in the tissue alterations. Indeed, evidence now available implicates the participation of a plethora of mechanisms, all of which appear to be interrelated in a complex way. The major aim of our endeavor is to elucidate further the various possible mechanisms underlying the pathologic alterations and to begin to determine which of these actually participate in the induction and evolution of plaque-associated gingival and periodontal disease in man. Specifically, we wish to elucidate the mechanism by which plaque accumulation leads to loss of the connective-tissue substance of the gingival tissues. Using modern techniques of molecular and cellular biology, we plan to evaluate mechanisms involving B- and T-lymphocytes, antibody, K-cells, macrophages, and antigen-antibody complex in the evolution of the disease.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $383,834

2.0095, REGULATION OF ANTIBODY RESPONSE

U.B. Storb, University of Washington, School of Medicine, Dept. of Microbiology & Immunology, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (P50 DE 02600-130023)

Our research is concerned with the genetic basis of antibody variability and with the regulation of antibody gene expression. The experimental tools include preparation of purified kappa-chain mRNA, preparation of complementary DNA by use of reverse transcriptase from avian myeloblastosis virus, DNA/RNA hybridization, cell-free translation, and cloning of synthetic and genomic immunoglobulin genes.

We have studied some parameters of the organization of immunoglobulin genes and found that immunoglobulin genes are transposed apparently somewhat independent of expression. We have also found that T lymphocytes contain immunoglobulin on RNA which is translatable, and that in B lymphocytes the quantity of immunoglobulin RNA increases with differentiation towards plasma cells. Further studies will be directed at the fine analysis of the organization of immunoglobulin genes by cloning and sequencing, and at the functional significance of immunoglobulin RNA in T lymphocytes.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$98,653

2.0096, THE ROLE OF COMPLEMENT IN THE PATHOGENESIS OF PERIODONTAL DISEASE

U.R. Nilsson, University of Pennsylvania, School of Dental Medicine, Dept. of Pathology, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (P50 DE 02623-120025)

The status of the complement (C) system in gingival crevice fluid (GCF) from individuals with and without periodontal disease will be studied. Main emphasis will be on C3 and C5, two key components in C-mediated inflammation. C3 and C5 and their possible cleavage products generated in GCF will be compared and contrasted with highly purified C3 and C5 and their biologically active cleavage products generated under carefully controlled conditions. A detailed physical-chemical analysis will be performed by gel filtration, sucrose density gradient, zone ultracentrifugation and by various modifications of the electrophoretic procedure. The analysis will be aided by the use of radioactively (125I) trace-labelled C proteins which also will be assayed immunochemically and functionally in tests for hemolytic, chemotactic and anaphylatoxic activities.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$109,117

2.0097, ROLE OF IMMUNITY IN PERIODONTAL DISEASE

A. Nowotny, University of Pennsylvania, School of Dental Medicine, Dept. of Periodontal Research, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (P50 DE 02623-120031)

Two microbes, the gram-positive Actinomyces viscosus (T14 V) and the gram-negative Eikenella corrodens (CS10-B), were selected for these studies since it has been shown independently by several laboratories that monoinfection with any one of the two will cause severe alveolar bone resorption in 10-14 weeks. Immunomodulating measures will be used to determine the role of immunity to these two microorganisms in the development of periodontitis-like lesions in germfree rats. If these bacteria and their products cause tissue destruction, immunization against them may prevent the lesions. Immunosuppression will facilitate disease development. On the other hand, if hypersensitivity (cell mediated immunity) to the microorganisms causes tissue destruction, immunosuppression will prevent the development of the lesions. Artificial hypersensitization or plain immunization may in that case enhance the rate of disease advancement.

As immunomodulating measures the following experimental series will be used: 1. Immunization with live or killed A. viscosus or E. corrodens vaccines. 2. Vaccination with added immunopotentiators. 3. Hypersensitization with microorganisms. 4. Passive immunization with high titer antisera to the microorganisms, and 5. Immunosuppression using irradiation and immunosuppressive drugs.

In all these animals the humoral as well as the cell mediated immune responses to the infectious agents will be measured longitudinally. Also, a longitudinal study of disease development will be recorded, comparing the rates of development. Inferences will be drawn regarding: 1. The role immunity may play in the pathogenic mechanisms of the disease, and 2. Possibly useful preventative and therapeutic modalities.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$101,110

2.0098, STUDIES OF THE STRUCTURE OF HUMAN SECRETORY IGA

J.F. Mestecky, University of Alabama in Birmingham, School of Dentistry, Dept. of Microbiology, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130018)

The overall objective of this research effort is to determine the cellular basis of induction of a secretory immune response, with specific emphasis on the oral bacterium Streptococcus mutans, a principal agent in the etiology of dental caries. The specific objectives are to elucidate the functional roles of lymphoid cells involved in the induction of both primary and anamnestic IgA immune responses, the potential influence of mediators on these responses, the origin of immunoglobulin-producing cells in secretory tissues, and the mechanisms involved in the homing of antigen-stimulated T and B cells.

Future research will be directed toward understanding the cellular basis of induction of a secretory immune response; toward determining the role of macrophages and T and B cells and their soluble mediators in the induction of IgA immune response; and toward determining the effect of adjuvants in augmenting the response.

This research concerns secretory immunity and the protective role of secretory antibodies.

The following will be investigated: 1. The mechanism of homing of IgA precursor cells on the colostral cell model. 2. The influence of endotoxin on cellular mechanisms involved in the induction of secretory immune response. 3. Further, the cross-protecting antigens of certain S. mutans in their protection against dental caries. 4. The induction of secretory response to various antigens orally ingested.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$199,494

2.0099, GRANULOCYTE GROWTH AND DIVISION

R.T. Parmley, University of Alabama in Birmingham, School of Dentistry, Dept. of Pathology, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130035)

This laboratory has been primarily involved in two projects. One project has been the investigation of ultrastructure and cytochemistry of leukocyte growth and diversion in normal and pathologic conditions. The other project has been an investigation of the ultrastructure and cytochemistry of iron and lead metabolism with the following objectives: 1. To develop cytochemical and autoradiographic techniques for the ultrastructural identification of iron and lead. 2. To identify mechanisms for normal and pathologic deposition of tissue iron and lead. 3. To determine the subcellular location of iron release from transferrin. 4. To determine the pathway and mechanism of iron and lead uptake in duodenal absorptive cells.

The cytochemical results obtained for rabbit and human granulocytes will be used as a normal comparison in studies of granulocyte disorders.

The data obtained for iron and lead uptake by duodenal epithelial cells will be compared to results obtained in other cell types using similar methodologies.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$178,949

2.0100, ABNORMALITIES OF MACROPHAGE-LYMPHOCYTE INTERACTION AS A PERIODONTAL FACTOR IN DEVELOPMENT OF PERIODONTAL DISEASE - A LONGITUDINAL STUDY

D.E. Lopatin, University of Michigan, Ann Arbor Campus, School of Dentistry, *Ann Arbor, Michigan* 48104 (P50 DE 02731-130035)

Specific periodontal disease associated bacteria and their subfractions, including: Actinomyces viscosus and Bacteroides melaninogenicus, will be examined for their ability to modulate in vitro cell mediated (CMI) and humoral immunity (antibody synthesis). These studies will examine their influence on regulatory lymphocytes, i.e. suppressor T-cells, and the influence of the regulatory cells on lymphocytes stimulated with the same bacterial components. The human populations to be examined will include: healthy individuals, in order to assess normal regulatory mechanisms affecting the response to oral antigens; periodontitis patients undergoing treatment, in order to determine if there are changes in the normal regulatory mechanisms that might predispose those patients to the disease; and populations being treated for gingivitis or periodontitis with mechanical and/or anti-microbial therapy, in order to assess effects of selective elimination of microbial flora on immune response and regulation. In addition, those patients in the current longitudinal study in order to assess long-term effects of periodontal disease treatment on immune response to oral antigens. In this manner, we will attempt to identify parameters of lymphocyte response to oral antigens that correlate with remission or exacerbation of the disease. This may also shed light on the question of whether the immune parameters associated with the disease actually contribute or are simply effects of the disease process.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$106,789

2.0101, HOST IMMUNOLOGIC RESPONSE TO ORAL MICROORGANISMS

P. Stashenko, Forsyth Dental Center, Dept. of Immunology, *140 Fenway St., Boston, Massachusetts* 02115 (P50 DE 04881-030003)

The host immunologic response to oral microorganisms may play a significant role in the pathogenesis of periodontal diseases. It is not clear whether this response is primarily protective or at times may have destructive components. In the present investigation, the humoral and cellular immunologic response to the predominant microorganisms isolated from sites of active destruction will be determined. Samples of saliva, blood, and gingival tissue from the diseased site(s) will be collected prior to and after therapy. Individual microbial species present in destructive and nondestructive sites will be compared for their relative ability to stimulate local and/or systemic cellular/humoral immune responses.

Reactions to a standard battery of suspected periodontopathic microorganisms will also be determined to provide some cross-sectional information between various patients in the studies. However, the priority analyses will be to antigens of the host's indigenous microbiota. Computer-assisted analyses of changes in immunologic responses will be compared to changes in microbial composition and clinical status of disease. Also, the effect of both mechanical and/or antibiotic therapy on these responses will be determined longitudinally for the individual patients.

Any consistent patterns in immunologic responses to the microbial antigens may be useful in determining etiologic agent(s) of specific periodontal diseases. It is conceivable that immunologic responses may reflect altered host-microbe interactions that precipitate the onset of disease. Thus, the use of changes in antibody levels or in cellular immune responses to suspected pathogens as an in vitro laboratory diagnostic test can be evaluated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$148,000

2.0102, PERIODONTAL DISEASE AND THE ELECTROMYOGRAPHIC SILENT PERIOD (HUMAN)

R.J. Genco, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (P50 DE 04898-030004)

SPECIFIC AIMS: The applicants hypothesize that periodontal involvement will comprise the ability of the receptors in the periodontal ligament to provide the usual inhibition to the motoneuron pool following a tap to the involved tooth. The aim of this project is to test this hypothesis by comparing the silent period duration in normal subjects and various types of periodontally diseased patients.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$124,224

2.0103, CLINICAL RESEARCH CENTER FOR PERIODONTAL DISEASE - IMMUNOLOGIC STUDIES

J.G. Tew, Virginia Commonwealth University, School of Basic Sciences & Graduate Studies, Dept. of Microbiology, *901 W. Franklin St., Richmond, Virginia* 23284 (P50 DE 05139-020002)

This project studies immunologic aspects of humans with defined periodontal conditions. A group of young adults with severe periodontitis (generalized) has been shown to be hyperresponsive to the polyclonal B-cell stimulant, Staphylococcal protein A. Several oral bacteria have been shown to have polyclonal B-cell activation (PBA) capability. Testing of other defined periodontal conditions in this system has begun. We will continue to identify oral organisms containing PBA, attempt to isolate and identify them, and study interactions of different PBA's. We have had initial partial success in lymphocyte-freeze storage experiments; these experiments will continue in attempts to remedy some loss of activity to antigen stimulation; very little, if any, loss of activity occurs when the stimulant is a mitogen.

Experiments indicating that antibody may be functional in the alternate complement pathway have been done and will be continued. We will attempt to determine if individuals with PMN chemotactic defects (see project 0003) also have hyperresponsiveness to PBA's, or whether the two laboratory findings occur in the same or different clinical groupings.

Scientific Classification Code: 20314

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$211,372

II. PERIODONTAL DISEASE

2.0104, ORAL BACTERIAL PRODUCTS AND BONE RESORPTION

E. Hausmann, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (R01 DE 01932-14)

The overall objective is to identify and describe, at a fundamental level, the biological mechanisms relating bacterial products in plaque and gingival debris to alveolar bone resorption in periodontal disease. Primarily a bone tissue culture model using chemically-defined media will be used. Bone resorption will be assessed quantitatively by the release of previously incorporated 45Ca from paired test and control bones from 19-day-old fetal rats. We also are attempting to develop a monkey model for periodontitis using 125I absorptiometry as a highly sensitive and nondestructive technique to assess alveolar bone loss.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

2.0105, IMMUNOPATHOLOGY OF GINGIVITIS AND PERIODONTITIS

R.J. Nisengard, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Periodontology, *3435 Main St., Buffalo, New York* 14214 (R01 DE 03408-07A1)

The release of the collagenase activating factor from mast cells will be investigated by determining changes in collagen after incubation with inactive tissue collagenase and supernates of challenged mast cells. Mast cells will be challenged by IgE mediated responsed, immune complexes and oral bacteria.

Immune complexes can cause osteoclastic activity. Human gingival tissue extracts will be examined by the Raji assay for immune complexes.

The role of in vivo coating of subgingival bacteria with immunoglobulins and complement in te modulation of the bacteria will be considered. Immunofluorescence will be employed to identify specific subgingival bacteria, the percentage coated with immunoglobulins and complement and serum antibody titers to the specific bacteria.

Sera and biopsies from patients with desquamative gingivitis will be examined by immunofluorescence to elucidate the role of these tests in the diagnosis of this disease.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $48,909

2.0106, IMMUNE PHENOMENA IN EXPERIMENTAL PERIODONTAL DISEASE

M.A. Taubman, Forsyth Dental Center, Dept. of Immunology, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 03420-07)

This proposed research will seek to define the role of cell-mediated immunity (CMI) and the secretory IgA immune system in the establishment of experimental periodontal disease in gnotobiotic rats. We have proposed to explore the nature of these roles utilizing a series of experiments in which CMI or the IgA system will be enhanced or ablated. The research plan has six major directions for study: (1) Enhanced CMI by antigen injection; intact IgA. (2) Ablated CMI and reduced IgA in neonatally thymectomized rats. (3) Ablated IgA using anti-heavy chain reagents with intact CMI. (4) Ablated CMI, reduced IgA in neonatally thymectomized rats with serum IgG antibody stimulated by systemic injection. (5) Enhanced IgA, by antigen feeding, without alteration of cellular immune status. (6) Enhanced CMI by the transfer of sensitized T lymphocytes.

A combination of immunologic techniques will be employed in these investigations. Peripheral sensitization will be determined by lymphocyte blastogenesis. T and B cells will be identified in gingival cell suspensions with specific fluoresceinated reagents. Antibody responses will be determined by an indirect ELISA technique.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $90,007

2.0107, ULTRASTRUCTURE OF EXPERIMENTAL PERIODONTITIS

P.R. Garant, State University of New York, Health Science Center at Stony Brook, School of Dentistry, Dept. of Oral Biology & Pathology, *Stony Brook, New York* 11790 (R01 DE 03745-08)

Based upon our previous studies of the pathogenesis of periodontal disease in mono-infected rats and our current histometric and electron microscopic investigation of periodontal disease in conventional rats we propose to continue morphometric studies of the inflammatory infiltrate with special emphasis on fibroblastic changes which are thought to be of importance in connective tissue remodelling. Particular emphasis will be placed on intracellular collagen fibrils (ICC) and on the recently discovered cell polarity of fibroblasts and their movement within the periodontal ligament. The increase of fibroblast ICC and contact with lymphocytes and osteoclasts will be investigated since preliminary data indicate that such a relationship exists. EM autoradiography, cytochemistry freeze-fracture and in vitro techniques will be used to provide an integrated view of fibroblast function in the gingiva and PDL. A mouse model of periodontal disease will be studied in the 'crinkled' strain placed on a high sucrose diet. Use of this system will permit EM autoradiographic studies of cell function in periodontal disease.

We propose to continue immunocytochemical localization of Actinomyces surface antigen and corresponding antibody in the oral tissues of gnotobiotic rats monoinfected with Actinomyces naeslundii and A. viscosus. We hope to be able to relate the penetration of actinomyces surface antigens to cell and tissue changes within the periodontium.

Part of this research plan will be concerned with elucidation of the role of fibroblasts in the maintenance of the principal fibers of the gingiva and the PDL. Based on our recent findings we suspect that active cell migration on existing principal fibers as a template is a necessary component needed to maintain the structural integrity of the PDL, while still permitting active turnover. This 'template' is destroyed during periodontal disease--thus full regeneration is difficult and perhaps impossible.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $103,975

2.0108, LEUKOCYTES IN THE PATHOGENESIS OF PERIODONTAL DISEASE

N.S. Taichman, University of Pennsylvania, School of Dental Medicine, Dept. of Pathology, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (R01 DE 03995-05)

The major objective of the work in progress is to identify and define some of the inflammatory mechanisms involved in periodontal disease(s). The emphasis is placed on the role of polymorphonuclear leukocytes (PMN) and related factors such as complement. The clinical approach to this problem consists of the study of the changes in various parameters of inflammation during experimental gingivitis and pre- and post-therapy in cases of more advanced periodontal disease. Parameters that are being measured are changes in PMN numbers, cell surface markers and function in the blood and saliva, changes in complement component profiles in serum and gingival fluid; changes in the PMN chemotactic system, both cellular and humoral; and changes in the lymphocyte response to a variety of plaque antigens and mitogens. The disease state in all cases is being monitored by a variety of clinical indices. These studies should enable us to construct functional profiles of PMN responsiveness in gingivitis and other periodontal disease(s) and will provide insight into the role of PMNs in disease. Studies on the effect(s) of PMNs and lymphocyte function and lymphocytes on PMN function are also underway. These experiments are designed to give us an insight into understanding the potential significance of inflammatory cell interactions in such inflammatory lesions as those seen in periodontal disease(s).

BIBLIOGRAPHIC REFERENCES: Baehni, P.C., Norman, M.E., Tsai, C.C., Stoller, N., McArthur, W.P. and Taichman, N.S.: Studies on host responses during experimental gingivitis. I. PMN responses to autologous plaque during the development of gingival inflammation. J. Perio. Res., in press, 1979.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $178,870

2.0109, MIF LYMPHOKINE INVOLVEMENT IN PERIODONTAL DISEASE

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A large body of evidence indicates that pharmacologically active lymphokines produced by antigen stimulation of immune lymphocytes regulate and amplify immune responses as well as the destruction associated with some disease states. Recent studies have now suggested that the gingival and bone destruction characteristic of periodontal disease are caused by lymphokines produced by dental plaque stimulation of immune thymus (T)- and bone marrow (B)-derived lymphocytes. Evidence for this presumption has been limited to qualitative tissue culture studies of lymphokine activities.

This proposal seeks to elucidate and define the role(s) of one lymphokine, human leukocyte migration inhibition factor (MIF), in periodontal disease. Efforts will be made to quantitate the in vitro plaque-induced MIF production by immune T and B cells as well as by assessing MIF levels in diseased gingival biopsy specimens in relation to the clinical severity of periodontal disease in the donor. The initial experimental thrust will be to isolate and purify MIF from T and B cell culture supernatants by the isoelectric focusing technique. Secondly, these purified preparations will be used for immunization to induce specific anti-MIF lymphokine antibodies. These antibodies will provide an immunologic tool to quantitatively assay the amount of MIF produced by plaque-stimulated lymphocyte cultures and in gingival tissue. The feasibility of the proposed methodology has been confirmed by the principal investigator during participation in the successful isolation and characterization of human T and B lymphocyte-derived monocyte chemotactic lymphokines. Also there are plans to investigate the functional role of MIF in plaque-induced T and B cell primary and secondary responses.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

2.0110, LYMPHOCYTE-MEDIATED CYTOTOXICITY IN PERIODONTAL DISEASE

P.A. O'Neill, University of Texas, Health Science Center at Houston, Dental Branch, Dept. of Microbiology, *6515 Freeman, Houston, Texas* 77025 (R01 DE 04210-05)

It is currently held that lymphocytes are involved in the tissue and bone destruction associated with chronic periodontal disease in humans; however, the actual mechanism of interactions between lymphocytes and gingival fibroblasts which lead to this destruction are not known. The presence of a preponderance of bone marrow-derived (B) lymphocytes has been found in these lesions, and recent work has shown that peripheral blood B lymphocytes can be activated in vitro by binding of agents to their Fc and C3 receptors. These activated B lymphocytes produce lymphokines, including lymphotoxin which destroys gingival fibroblasts. It is thought that B lymphocytes may be thus activated in vivo.

This project proposal outlines studies for comparing the reactivities of peripheral blood lymphocytes and those isolated from gingival tissue in relation to gingival fibroblast destruction. This will be done using cytotoxicity assays with gingival fibroblast cultures. In addition, various means of activating B lymphocytes and amplifying their responses will be explored. Activating agents include antigen-antibody complexes prepared with antisera to dental plaque and oral bacteria, complement-binding agents, and soluble factors from activated cells. The final phase of the program will focus on collagen synthesis and secretion by gingival fibroblasts in contact with lymphocyte populations to assess whether there may be impairment of these functions.

It is hoped that these studies of the consequences of interaction of the immune system with gingival fibroblasts in chronic periodontitis may give us an indication of the mechanisms involved in tissue destruction and may lead to ways of preventing or retarding this process in human periodontal disease.

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SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $33,070

2.0111, SEVERE PERIODONTITIS - IMMUNOLOGIC STUDIES

R.R. Ranney, Virginia Commonwealth University, School of Dentistry, Dept. of Periodontics, *901 W. Franklin St., Richmond, Virginia* 23284 (R01 DE 04397-03)

This project investigates the significance of immunologic factors in periodontal disease. Indicators of general immune capacity and specific immune response to antigens common to dental plaque will be compared between persons with severe periodontitis and those with a healthy periodontium. All subjects will be free of systemic disease as determined by a thorough medical evaluation. Their periodontal status will be characterized fully, using standard indices and a total attachment loss index. Their general immunologic status will be evaluated by assessing serum immunoglobulins and complement components with radial immuno-diffusion, blastogenesis of peripheral lymphocytes stimulated by mitogens, levels of T- and B-lymphocytes by rosette formation, capacity to mount dermal hypersensitivity (Type IV) response, and phagocytic capacity of polymorphonuclear leukocytes. Specific immunity will be assessed by serum antibody levels, blastogenesis and lymphokine synthesis by lymphocytes and dermal hypersensitivity related to antigens derived from dental plaque organisms.

Difference in any of the immune measures between experimental and control subjects will be sought and pursued when found.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0112, CELL MEDIATED IMMUNITY GINGIVAL INFLAMMATION (2)

B. Macedo Sobrinho, College of Medicine & Dentistry of New Jersey, New Jersey Dental School, School of Dentistry, Dept. of Oral Biology & Pedodontics, *100 Bergen St., Newark, New Jersey* 07103 (R01 DE 04501-04)

The overall objective of this proposal is to contribute to a greater understanding of the cellular elements involved in the prevention and in the pathogenesis of periodontal disease by continuing to investigate the participation of cell mediated immune phenomena occurring in the tissues affected by periodontal inflammation. Numerous experiments suggest that the understanding of the interplay between immune cells and the cells of the periodontium is essential to progress in this investigative area.

Specifically, this proposal seeks support to delineate the role that suppressor factor(s) from thymus derived theta positive cells play on mouse gingiva. Established techniques of immune reconstitution along with histological procedures will be employed to determine whether the administration of suppressor factors to dinitrofluorobenzene immunized mice will alter the course of periodontal tissue breakdown.

BIBLIOGRAPHIC REFERENCES: Macedo-Sobrinho, B., Ramras, H., and Yablonicky, C.: 'Gingival Tolerance to Dinitrofluorobenzene (DNFB) in Mice', International Association of Dental Research 252, 1978. Macedo-Sobrinho, B., Roth, G., and Grellner, T.: 'A Tubular Device for Intraoral Examination of Rodents', Journal of Laboratory Animal Science - in press, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$28,429

2.0113, ROLE OF THE IMMUNE SYSTEM IN PERIODONTAL DISEASE

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The role of the immune system in the pathogenesis of periodontal disease will be studied. The common oral microorganism Actinomyces viscosis will be used to orally infect and produce periodontal lesions in inbred mice. The incidence and extent of the disease process will be studied in thymus lymphocyte-deficient mice, bone marrow lymphocyte-deficient mice and normal control mice. The degree of disease produced in each group of mice will be determined by measuring bone loss and the nature of the inflammatory infiltrate in the soft tissues. The general and specific immunologic competence of the animals will be studied. Measurement of both T- and B-cell responsiveness to A. viscosis antigens will be performed and related to the occurrence and severity of the disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0114, CELL-MEDIATED IMMUNITY IN PERIODONTAL DISEASE

S.T. Sonis, Harvard University, Boston Campus, Peter Bent Brigham Hospital, *721 Huntington Ave., Boston, Massachusetts* 02115 (R01 DE 04677-03)

Previous studies indicate that cell-mediated immunity (CMI) plays significant role in the pathophysiology of periodontal disease. These studies have measured varied cell-mediated immune responses of peripheral blood leukocytes to dental plaque antigen. It appears that the distribution of the local gingival leukocyte population is different from that found in peripheral blood. Additionally, the local gingival environment is rich in factors that are known to modify cell-mediated immunity and leukocyte to leukocyte interaction. Therefore, the response of gingival crevice leukocytes to plaque antigens may be significantly different from that mediated by peripheral blood leukocytes. Similarly, gingival crevice leukocytes may be susceptible to serum elements which can modify CMI. The objectives of the proposed study are to compare the immune characteristics and functional relationships of gingival crevice leukocytes with peripheral blood leukocytes. Populations of gingival crevice and peripheral blood leukocytes will be studied for metabolic activity in patients with known neutrophil and periodontal abnormalities and activity will be correlated with level of disease. Immune complexes of known composition will be tested for their ability to modify both gingival crevice and peripheral blood leukocyte function and for their ability to effect leukocyte interactions. Modification of lymphocyte function by plaque and antigen activated neutrophils will be studied for populations of gingival crevice and peripheral blood cells. The functional effect of neutrophils on lymphocytes will be examined and the chemical nature of neutrophil-derived lymphocyte activators will be determined. The concentration of activating factors in the gingival crevice will be quantified as will the ability of gingival crevice leukocytes to produce such a factor.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$65,447

2.0115, CELLULAR INFILTRATES IN HUMAN PERIODONTAL DISEASE

B.F. Mackler, University of Texas, Health Science Center at Houston, Dental Branch, *6515 Freeman, Houston, Texas* 77025 (R01 DE 04762-01)

The inflammatory cellular infiltrates found in human gingival tissue are presumed to mediate the pathogenesis of periodontal disease. However, the nature of the host defense mechanisms involved in the destruction of gingival tissue and alveolar bone remain unclear. In vitro studies of dental plaque and microbial antigen-stimulated human peripheral blood lymphocytes have suggested roles for cellular and humoral responses as well as for immune complexes. These studies are only presumptive since they examined peripheral blood lymphocytes.

This proposal seeks to define, in situ, then isolate and functionally characterize the immunologic and nonspecific effector responses of lymphocytes present in periodontal lesion cellular infiltrates. The first experimental approach will be to characterize cellular infiltrates of periodontal lesions in situ by morphological, cytochemical, and immunopathological assessments. These studies will seek to define distinct features of inflammatory cellular infiltrates which correlate with independently assigned clinical disease categories - mild gingivitis, severe gingivitis, and periodontitis. The second experimental approach will be to recover gingival lymphocytes, and other inflammatory cells, from diseased gingiva, then characterize these cells using cell surface markers. These results should correlate with and extend the in situ findings as well as provide direction for the functional characterization studies. Thirdly, the in vitro effector responses presumed to be correlates of the in vivo disease will be assessed using isolated gingival lymphocytes which are effector cells actively involved in the pathogenesis of human periodontal disease. These functional evaluations will include immune lymphocyte blastogenesis, lymphokine production, cytotoxicity for gingival fibroblasts and antibody production. In addition, the regulatory roles of serum factors, immune complexes, and certain lymphoid subpopulations on these gingival lymphocyte effector responses will also be investigated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0116, POTENTIAL ROLE OF COMPLEMENT IN GINGIVAL INFLAMMATION

U.R. Nilsson, University of Pennsylvania, School of Dental Medicine, Dept. of Pathology, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (R01 DE 04809-02)

The status of the complement (C) system of gingival crevice fluid (GCF) from periodontal inflammatory lesions is compared with that of normal serum and of GCF from periodontal tissue with minimal inflammatory involvement. The cleavage of C3 and C5 serves as a parameter of C activation and possible inflammatory involvement. Comparisons are made between the cleavage patterns seen in C3 and C5 derived from GCF and those obtained with highly purified 125I trace labelled C3 and C5 incubated with GCF in vitro. A detailed physical-chemical analysis is performed by gel filtration, sucrose density gradient ultracentrifugation and by electrophoretic procedures. Highly specific antisera to C3, C5, lysosomal enzymes and to serum protease inhibitors help define immunochemically various C fragments as well as the enzymes causing C cleavage. The functional analysis employed in the definition of the C fragments include hemolytic, chemotactic and anaphylatoxic assays.

The information gained by these studies may help us understand the involvement of C as a pathogenetic factor in periodontal disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$105,025

2.0117, SPECIFICITY OF CMI RESPONSE IN PERIODONTAL DISEASE

M.J. Reed, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (R01 DE 04988-01)

The basis of this research is to investigate the specificity of the cell-mediated immune response in periodontal disease. A relationship has been established between the host's cell-mediated immune response to certain oral bacterial antigen preparations and the periodontal disease status of the individual. The ubiquitous and non-life threatening nature of periodontal disease affords the opportunity to carry out specificity studies in a human disease state with a known CMI component. The antigens to be used in this study will be purified from a sonicate supernatant preparation from Actinomyces viscosus (ATCC 19246). The biological activity of the purified antigen(s) will be assessed using in vitro lymphocyte blastogenesis using host peripheral blood lymphocytes as the target cell population. The chemical composition of the antigen(s) will be determined. The specificity studies with pure antigen will be designed to determine the molecular biology of the interaction of antigen with specifically sensitized cells. The initial approach will be to subject the purified antigen to controlled pronase and/or trypsin digestion. The resultant subunits will be separated by appropriate column chromatography procedures and tested in the in vitro assay system. Active subunits will be further characterized with regard to chemical composition. Delineation of the specific antigenic site on the subunit will be carried out using specific enzymatic or chemical modification of the subunits with subsequent analysis of activity.

The determination of the specificity of the hosts CMI response in human disease state in which the disease may be of short or long-term duration and readily controlled will contribute significantly to the role of this type of immune response in the pathology of the disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$55,707

2.0118, OCCURRENCE AND ANTIGENICITY OF ENAMEL PROTEINS

S.E. Schonfeld, University of Southern California, School of Dentistry, Dept. of Microbiology & Immunology, *3551 University Ave., Los Angeles, California* 90007 (R01 DE 05088-02)

Studies which were undertaken by the principal investigator demonstrated that: 1. Enamel Proteins seem to be a component of 'root analogue' surfaces on specialized teeth (the lingual surfaces of the rabbit incisor). Preliminary evidence indicates that these proteins are also present on forming root surfaces of mouse molars, and 2. That enamel proteins are capable of eliciting autoimmune responses both in vitro an in vivo. The present proposal seeks funding to answer the following three questions: 1. Are enamel proteins present on the root surfaces of primate teeth? 2. What is the relationship between the occurrence and antigenicity of enamel proteins to the pathogenesis of periodontal disease? 3. What is the nature of the autoimmune response to enamel proteins in vitro?

An antiserum to enamel proteins from developing primate or human teeth will be raised in rabbits according to an established protocol (Schonfeld, J. Dent. Res. 54:C72, 1975; Schonfeld, Trump, and Slavkin, Proc. Soc. Exp. Biol. Med., In Press). This antiserum will be used to look for substances which cross-react with enamel proteins on the root surfaces of primate or human teeth by radioimmunoassay, immunoelectrophoresis, and fluorescence microscopy. The participation of an enamel protein-associated autoimmune response in the pathogenesis of clinical periodontitis will be investigated by comparing lymphocyte transformations of normal and periodontal disease patient's lymphocytes in response to enamel proteins in vitro, and by checking for antibodies to enamel proteins in the sera of periodontal disease patients by immunofluorescence microscopy. The nature of the in vitro immune response will be investigated to determine whether the reaction is strictly T-cell dependent using a T-cell deficient mouse and anti-thymocyte serum. Further studies will determine if the autoimmune response to enamel proteins become more severe during the aging of NZB mice.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$55,695

2.0119, IMMUNOCHEMICAL STUDIES IN PERIODONTAL DISEASE

B.J. Mansheim, State University System of Florida, University of Florida, School of Medicine, Dept. of Medicine, *1600 Archer Rd., Box J-266, Gainesville, Florida* 32610 (R01 DE 05352-01)

Bacteroides melaninogenicus has been shown to play an essential role in certain mixed anaerobic infections. It has further been ascribed a role as a dominant pathogen in certain types of periodontal disease and has been shown to induce rapidly advancing periodontal disease when introduced in a pure inoculum into germ-free rats. We propose to study the cell surface antigens of B. melaninogenicus. We have successfully isolated, purified, and partially characterized the major antigens using gel chromatography and various immunochemical techniques. Using purified antigens we have begun to study the humoral immune response in animals infected by B. melaninogenicus, by means of sensitive radioactive antigen binding assay. Specific studies will be conducted utilizing a germ-free rat model, where organisms can be introduced in a controlled fashion, thereby facilitating the interpretation of immunologic data. Serologic tests will be developed, using purified antigens for potential use in defining serogroups within this species, and as rapid diagnostic methods for determining the presence of B. melaninogenicus in clinical infection. Ultimately, we propose to study the potential for use of these purified antigens as vaccines for the protection against oral infections by B. melaninogenicus, specifically periodontal disease.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $58,505

2.0120, CHARACTERIZATION OF CELLULAR INFILTRATES IN HUMAN PERIOD

B.F. Mackler, University of Maryland, Baltimore Professional Schools, School of Dentistry, Dept. of Pathology, *66 W. Baltimore St., Baltimore, Maryland* 21201 (R01 DE 05612-01)

The inflammatory cellular infiltrates found in human gingival tissue are presumed to mediate the pathogenesis of periodontal disease. However, the nature of the host defense mechanisms involved in the destruction of gingival tissue and alveolar bone remain unclear. In vitro studies of dental plaque and microbial antigen-stimulated human peripheral blood lymphocytes have suggested roles for cellular and humoral responses as well as for immune complexes. These studies are only presumptive since they examined peripheral blood lymphocytes.

This proposal seeks to define, in situ, then isolate and functionally characterize the immunological and nonspecific effector responses of lymphocytes present in periodontal lesion cellular infiltrates. The first experimental approach will be to characterize cellular infiltrates of periodontal lesions in situ by morphological, cytochemical, and immunopathological assessments. These studies will seek to define distinct features of inflammatory cellular infiltrates which correlate with independently assigned clinical disease categories - mild-gingivitis, severe gingivitis, and periodontitis. The second experimental approach will be to recover gingival lymphocytes, and other lymphocytes, and other inflammatory cells, from diseased gingiva, then characterize these cells using cell surface markers. These results should correlate with and extend the in situ findings as well as provide direction for the functional characterization studies. Thirdly, the in vitro effector responses presumed to be correlates of the in vivo disease will be assessed using isolated gingival lymphocytes which are effector cells actively involved in the pathogenesis of human periodontal disease. These functional evaluations will include immune lymphocyte blastogenesis, lymphokine production, cytotoxicity for gingival fibroblasts and antibody production. In addition, the regulatory roles of serum factors, immune complexes and certain lymphoid subpopulations on these gingival lymphocyte effector responses will also be investigated.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $42,673

2.0121, CELLULAR IMMUNE RESPONSES TO ORAL BACTERIAL ANTIGENS

P.B. Chen, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (R23 DE 04953-02)

The induction of cellular immune responses to antigens prepared from oral bacteria associated with periodontal disease is being studied using two in vitro techniques: lymphocytes blastogenesis and the Jerne antibody producing cell (PFC) assay. Antigens are being prepared from Actinomyces viscosus and Bacteroides asaccharolyticus. An unrelated antigen, sheep red blood cells, is used in the Jerne PFC assay.

Soluble antigens from A. viscosus are prepared by sonication and subsequent fractionation on Bigel P-300 or DEAE. Cell walls of A. viscosus are obtained after sonication. Soluble antigens are prepared from B. asaccharolyticus by sonication. Cell walls will be obtained and the lipopolysaccharide extracted.

Blastogenic responses of human peripheral blood and tonsil lymphocytes to the bacterial antigens will be assayed to determine the presence of antigenic components and/or mitogenic components. Subpopulations of human peripheral blood lymphocytes will be similarly tested.

We have demonstrated that A. viscosus has adjuvant activity in a mouse spleen cell system. We will also test for antibody production to antigen fractions of A. viscosus in mice that have been immunized with A. viscosus and/or B. asaccharolyticus. Human peripheral blood and tonsil lymphocytes will similarly be tested for their ability to produce antibody to A. viscosus and/or to B. asaccharolyticus, and to fractions of these antigens.

BIBLIOGRAPHIC REFERENCES: Chen, P., Doroszczak, N. and Genco, R.J., Cellular immune responses to Actinomyces viscosus: species differences. (Abstract). Fed. Proc. 37: Abs. 3143, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$28,912

2.0122, MACROPHAGE AND FIBROBLAST PROLIFERATION IN VITRO

R.B. Rutherford, Virginia Commonwealth University, School of Dentistry, Dept. of Periodontics, *901 W. Franklin St., Richmond, Virginia* 23284 (R23 DE 05355-01)

This project should contribute to an improved understanding of relationships between the cellular exudate of inflammation and concomitant tissue destruction and repair by studying the capacity of human monocyte/macrophages to alter the growth of human fibroblasts.

Purified human peripheral monocytes are cultured under defined conditions in vitro. The medium supporting the monocytes is transferred to fibroblasts in stationary phase (quiescent) and the effects on the number of attached fibroblasts are measured over time. Since the medium supporting the monocytes is totally defined, isolation of substances elaborated there by the cells should be facilitated. Such isolations and subsequent characterizations will be carried out.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0123, LEUKOCYTE SUBPOPULATIONS FOR PRODUCTION OF OSTEOCLAST ACTIVATING FACTOR AND BONE RESORPTION

C.E. Hawley, U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research, *Washington, District of Columbia* 20012 (Y01DE60025 (CONTRACT))

OBJECTIVES AND WORK SCOPE: This project proposes to determine the role of human lymphocytes and macrophages in the production of the 'osteoclast activating factor (OAF).' Specifically (a) establishment of a precise role for T- and B-lymphocytes, their subpopulations, and monocytic macrophages in the generation of OAF, (b) confirmation of the isolation and identification of bone resorbing products found in the culture media to be sure OAF is the factor being formed, (c) determination that OAF is generated by using compounds that inhibit bone resorption due to other bone resorption-stimulating factors.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$96,247

2.0124, MECHANISMS OF HISTAMINE RELEASE

R. Siraganian, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Clinical Immunology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00034-11 LMI)

Histamine release from mast cells and blood basophils is being studied as one of the immunological mechanisms involved in inflammation. Among the histamine releasing agents employed are IgE antibody, environmental antigens, and complement factors (C5a and C3a) derived from human serum. The relationships between EgE crosslinking, basophil desensitization and histamine release were analyzed by kinetic studies. Release of inflammatory mediators from cultured mastocytoma cells is being compared with mechanisms of release from mast cells and basophils.

BIBLIOGRAPHIC REFERENCES: Siraganian, R.P. and Harzard, K.A.: Mechanisms of mouse mast cell activation and inactivation for IgE-mediated histamine release. J. Immunol. 122:1719-1725, 1979. DeLisi, C. and Siraganian, R.P.: Receptor cross-linking and histamine release. I. The quantitative dependence of basophil degranulation on the number of receptor doublets. J. Immunol. 122:2286-2292, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$177,290

2.0125, MACROPHAGE AND LYMPHOCYTE MEDIATORS THAT AMPLIFY T AND B LYMPHOCYTE REACTIONS

J.J. Oppenheim, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Cellular Immunology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00045-08 LMI)

Human macrophages when activated by a variety of agents produce lymphocyte activating factor (LAF). LAF exists in a 15,000 mw form which when mixed with serum changes to a 60,000 mw form. Both forms of LAF are mitogenic for peanut agglutinin negative (PNA minus) mouse thymocytes. The higher mw form also induces increased Lyt-1 expression by thymocytes and is mitogenic for human T lymphocytes. Only the lower mw replaces macrophages in lectin induced human T cell proliferation and enhances helper T cell dependent immunoglobulin production by human B cells. The mitogenic effects of LAF can be competitively inhibited by allose. Human T lymphocytes can be activated by lectins or antigens to produce a mitogenic factor(s) (LMF). LMF is also mitogenic for mouse PNA minus thymocytes and elutes in the same two regions off Sephadex as LAF. LMF differs from LAF in that: 1) LMF production is inhibited by suppressor T cells, 2) The 15,000 mw LMF is mitogenic for human B cells as well as for cytoxic T lymphocytes and 3) LMF is not inhibitable by allose. Presumably LAr ana LMF amplify immunological reactions by promoting the growth and differentiation of distinct subpopulations of lymphoid target cells.

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SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$148,062

2.0126, ROLE OF LYMPHOCYTE AND MACROPHAGE MEDIATORS IN INFLAMMATION

S.M. Wahl, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Humoral Immunity Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00046-09 LMI)

Research in this laboratory focuses primarily on the role of lymphocytes and macrophages in the regulation of connective tissue metabolism associated with inflammatory reactions. Antigen specific activation of lymphocytes results in the production of biologically active lymphokines. One of these lymphokines has the ability to stimulate fibroblasts to divide and to increase their synthesis of both collagen and noncollagen protein. Another lymphokine, macrophage activation factor, activates macrophages. Macrophages also produce a molecule which enhances fibroblast function. Activation of macrophages by MAF and other stimulants involves prostaglandin generation and alterations in intracellular levels of cAMP. By these mechanisms the immune system may modulate connective tissue metabolism in inflammatory lesions.

BIBLIOGRAPHIC REFERENCES: Rosenstreich, D. L. and S. M. Wahl, 1979. Cellular source of lymphokines. In Biology of the Lymphokines. J. J. Oppenheim, and S. Cohen, eds.. Academic Press, New York, p. 209-242. Wahl, S. M., L. M. Wahl, J. B. McCarthy, L. Chedid and S. E. Mergenhagen. 1979. Macrophage activation by mycobacterial water soluble compounds and synthetic muramyl dipeptide. J. Immunol. 122: 2226.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$80,728

2.0127, CONTROL MECHANISMS OF IGE PRODUCTION

R. Siraganian, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Clinical Immunology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00114-05 LMI)

The control mechanisms of IgE production are under study utilizing a mouse model system. Attempts are being made to purify murine IgE and develop a radio-immunoassay capable of quantitating the small amounts of IgE present in mouse serum (estimated to be less than 1.0 micron/ml): for this purpose an IgE-hydriodoma has been produced. Mice exposed to nebulized antigens are incapable of an IgE response when later immunized with the same antigen. The mechanism of this phenomenon is under investigation.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $64,222

2.0128, REGULATORY ROLE OF THYMUS-DERIVED LYMPHOCYTES ON THE IN VITRO ANTIBODY RESPONSE

J.J. Farrar, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Cellular Immunology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00131-05 LMI)

Macrophages (M0) and T cells produce a variety of soluble factors which modulate the induction of the antibody and cell-mediated immune responses. The biochemical relationship between the multiple factors, their mode-of-action, and conditions under which they are produced have been investigated. Interleukin 2 (IL 2), which augments plaque-forming cell (PFC) and cytotoxic T cell responses, has been shown to be T cell-derived although M0-dependent. The M0 requirement during the production of IL 2 can be replaced by either phorb 1 myristic aceptate or M0 culture supernatants. Interleukin 1 (Il 1) (LAF) has been shown to be 1) produced in vivo, 2) capable of replacing the requirement for M0 during the induction of primary T cell responses and 3) capable of synergizing with a late-acting T cell replacing factor (TRF) in the induction of the antibody response. TRF has been shown to be distinct from the principal component of IL 2 on the basis of differential sensitivity to pH 2.0 and partial separation by hydrophobic chromatography. Thus at least three distinct immunoenhancing factors (IL 1, IL 2, and TRF) have been partially delineated biochemically and functionally. Studies are currently in progress to attempt to elucidate the mechanism by which these factors function in concert to enhance B cell and T cell responses.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $154,581

2.0129, THE BIOLOGICAL ACTIONS OF BACTERIAL ENDOTOXIN IN VIVO AND IN VITRO

D.L. Rosenstreich, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Cellular Immunology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00167-03 LMI)

The LPS-unresponsive C3H/HeJ mouse strain has been utilized to help elucidate the mechanism of action of bacterial endotoxin (LPS). These mice posses a defect in the LPS-responsiveness of their T and B lymphocytes, macrophages, and fibroblasts that is due to a mutation in single, autosomal co-dominant gene. The biological effects of LPS are cell mediated because the interaction of LPS with lymphocytes and/or macrophages renders C3H/HeJ mice susceptible to LPS-induced lethality, immunogenicity, adjuvanticity, and tumor necrosis, as shown by the adoptive transfer of bone marrow cells from LPS-sensitive mice. C3H/HeJ mice can also be rendered LPS-sensitive by preinfection with BCG, a potent immunostimultant. Endotoxicity may be mediated by a number of LPS-induced acute phase reactants such as prostaglandins, lymphocyte activating factor, interferon, colony stimulating factor, and serum amyloid associated protein which are detectable in the sera of LPS-sensitive animals. The LPS gene may also play a vital physiological role since it appears to control the ability of macrophages to manifest LPS-induced tumor cell killing as well as the ability of macrophages to respond to LPS in vivo and in vitro with the production of physiologically relevant cytokines.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$210,520

2.0130, INVESTIGATION OF CELLULAR IMMUNOLOGICAL MECHANISMS IN PERIODONTAL DISEASE

P.C. Fox, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Clinical Immunology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00205-03 LMI)

A group of patients with periodontosis is being studied to identify cellular immunologic deficiencies. They are being compared to patients with juvenile and adult periodontitis and individuals without periodontal pathology. A familial pattern of this disease is being investigated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$103,457

2.0131, BIOLOGICAL AND BIOCHEMICAL CHARACTERIZATION OF LYMPHOCYTE ACTIVATING FACTOR

S.B. Mizel, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Cellular Immunology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00209-03 LMI)

The mouse macrophage cell line, P388D, in conjunction with the potent inflammatory and tumor promoting agent, phorbol myristic acetate (PMA) have been used to obtain sufficient quantities of lymphocyte activating factor (LAF) for purification and characterization studies. LAF has been purified 10,000-20,000 X with a yield of 7 percent. Chemical studies have revealed the importance of argenine groups in LAF activity. Biological studies have demonstrated that LAF enhances: 1) thymocyte proliferation; 2) antibody synthesis in vitro; 3) the generation of alloantigen-specific cytotoxic T cells; 4) antigen-specific T cell proliferation; 5) the generation of stable E-rosette forming human T cells and 5) collagenase and prostaglandin production by rheumatoid synovial cells. Thus LAF may play an important, if not essential role in T cell activation for humoral and cell medicated immune responses as well as in inflammatory responses such as in the joints of patients with rheumatoid arthritis.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$81,541

2.0132, REGULATION OF MEDIATOR PRODUCTION IN ENDOTOXIN-STIMULATED MACROPHAGES

R.N. Moore, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Cellular Immunology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00238-02 LMI)

The controlling mechanisms which regulate production of inflammatory mediators by endotoxin stimulated murine macrophages are currently under investigation. Research has concentrated upon four important mediators; interferon, granulocytemacrophage colony stimulating factor (CSF), lymphocyte activating factor (LAF) and prostaglandins. Evidence obtained indicates that both prostaglandins and CSF may serve regulatory roles in mediator production by stimulated macrophages. E series prostaglandins (PGE) have been found to inhibit production of both CSF and interferon while CSF has been found to directly stimulate both PGE and LAF production by macrophages. Preliminary results suggest that CSF also sensitizes macrophages to endotoxin. CSF-cloned macrophages produced more interferon on a per cell basis than normal macrophages while normal macrophages preincubated with a source of CSF also responded in a hypersensitive manner. A partially purified CSF preparation has also been found to enhance LAF production by endotoxin-stimulated macrophages. Work in progress is designed to further investigate these oposing effects of PGE and CSF on macrophage functions.

BIBLIOGRAPHIC REFERENCES: McGhee, J. R., S. M. Michalek, R. N. Moore, S. E., and D. L. Rosenstreich, 1979. Genetic control of in vivo sensitivity to lipopolysaccharide: Evidence for codominant inheritance. J. Immunol. 122: 2052.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$118,249

2.0133, THE ROLE OF OXYGEN-DERIVED FREE RADICALS IN INFLAMMATION

J.T. Hoffeld, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Cellular Immunology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00242-02 LMI)

We have defined some of the effects of oxygen-derived free radical compounds (ODFRC) (viz, superoxide, hydroxyl, singlet oxygen and hydrogen peroxide) in inflammation by sing three in vitro models of inflammatory cellular interactions. We have shown that the radical scavenger, reduced glutathione is a major positive determinant of the ability of murine spleen cells to produced an antibody response, in vitro. We have found that the enhancement of the antibody response by 2-mercaptoethanol is also mediated by glutathione. These enhancement effects can be mimicked by the addition of other known scavengers of ODFRC. Macrophages, stimulated in vivo, can suppress lectin-induced lymphocyte proliferation and serum-induced fibroblast proliferation. The use of inhibitors of prostaglandin synthesis and scavengers of ODFRC has provided evidence that the suppression of lymphocyte proliferation by macrophages is produced by a synergy of prostaglandins and ODFRC; similar experiments have provided evidence that the suppression of fibroblast proliferation by macrophages is mediated by ODFRC alone. Thus ODFRC appear to be important in the modulation of inflammatory cellular interactions.

BIBLIOGRAPHIC REFERENCES: J. T. Hoffeld and J. J. Oppenheim. 1980. The capacity of fetal calf serum to support a primary antibody response in vitro is determined, in part, by its reduced glutathione content. Cellular Immunology (In press). Metzger, Z., J.T. Hoffeld and J.J. Oppenheim. 1980. Macrophage-mediated suppression: I. Evidence for participation of both hydrogen peroxide and prostaglandins in suppression of murine lymphocyte proliferation. Journal of Immunology (In press).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$91,052

2.0134, TUMOR CELL DERIVED IMMUNOSUPPRESSIVE FACTORS

S.B. Mizel, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Cellular Immunology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00259-01 LMI)

Murine sarcoma virus (MuSV) transformed mouse fibroblasts produce potent in vitro immunosuppressive factors (ISF). The partially purified ISF inhibited phytohemagglutinin (PHA) and concanavalin A (Con A) induced thymocyte proliferation, lipopolysaccharide (LPS)-induced spleen cell proliferation, the in vitro splenic anti-sheep red blood cell plaque forming cell response, and the generation of alloantigen specific cytotoxic T cells. The effect of ISF on thymocyte proliferation was not readily reversible and required only a 4 hr exposure of the thymocytes to ISF in order to inhibit cell proliferation. Although ISF shared several biochemical properties with a MuSV-transformed cell-derived sarcoma growth factor (SGF), e.g., acetic acid solubility, sensitivity to dithiothreitol, the two factors could be resolved by gel filtration on Bio-Gel P-60. Two peaks of ISF activity were found with apparent molecular weights of 12,000 and 8,000.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$47,824

2.0135, GENETIC CONTROL OF IMMUNOLOGIC MECHANISMS

D.L. Rosenstreich, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Cellular Immunology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00260-01 LMI)

Natural resistance to a number of infectious disease organisms in mice is under genetic control. The nature of these genes and the immune mechanisms that they control are being investigated. Resistance to Rickettsia Tsusugomushi, the agent of scrub typhus, is controlled by a single, dominant gene (RIC) that is located in the middle of chromosome 5. This gene controls some function that is operative within four hours after bacterial infection. Resistance to Salmonella typhimurium, the agent of typhoid fever is controlled by three genes: 1) an x-linked gene that controls B cell differentiation (xio), 2) the LPS gene and 3) a chromosome 1 gene (Ity) that may control some aspect of cell mediated immunity. Resistance to Herpes simplex virus-1, the causative agent of acute gingivostomatitis and recurrent herpes labialis, is also polygenic. The number, location and mechanisms controlled by these genes are currently under investigation. Characterization of the genes that control resistance to infectious organisms will facilitate identification of individuals susceptible to any given disease and enable the development of appropriate preventive or therapeutic measures.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$37,273

2.0136, UPTAKE OF PLAQUE ANTIGENS BY GUINEA PIG EPIDERMAL LANGERHANS CELL - AN IMMUNOFLUORESCENT AND HISTOCHEMICAL INVESTIGATION

D.M. Rafferty, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Leavenworth, Kansas* 66048 (686-001-P)

Assessment of uptake of plaque antigens by Guinea Pig epithelial utilizing indirect immuno fluoresence and histochemical (adenosine triphosphatase-ATP-ase) staining was attempted.

Supra and subgingival plaque was collected pooled, sonicated and formalin treated for vaccine preparation. The vaccine was separated into aliquots, injected combined with incomplete Freund's adjuvant into rabbits and the serum collected. Other aliquots were injected intradermally into guinea pig foot The guinea pig tissue was frozen sectioned and alternate 15 micra section were treated with either ATPase stain on rabbit antiserum followed by sheep anti-rabbit globulin conjugated with fluorescein isothicyanate.

Serum tests revealed presence of antibody to particulate antigen material. Comparison of fluorescent sections with APT-ase treated sections demonstrated no presence of antigen around or aithin the Langerhans cells.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0137, IMMUNE RESPONSES TO THE MICROBIAL FLORA OF DENTAL PLAQUE - THEIR RELATIONSHIP TO DEVELOPMENT OF PERIODONTAL DISEASE

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No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$20,103

2.0138, EXPERIMENTAL GINGIVITIS AND PERIODONTITIS IN MACAQUE MONKEYS

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The aims are to study the host tissue response in chronic gingivitis and periodontitis in these animals, with a view to elucidating the degree to which the components of the immune inflammation present are damaging or protective to the tissues.

Starting from a baseline in gingival health, induced by daily topical application of chlorhexidine gluconate, the development of gingivitis has been studied both clinically and in serial biopsies. The cell populations of the developing inflammatory infiltrate have been quantified and the proliferation rate of inflammatory cells aroused by tritiated thymidine labelling.

Similar approaches are now being applied to advanced destructive periodontal disease in normal animals and in animals immunosuppressed with steroids and axothioprine.

SUPPORTED BY

University of London	funds n.a.

2.0139, EXPERIMENTAL GINGIVITIS

W.J. Loesche, University of Michigan, Ann Arbor Campus, School of Dentistry, *Ann Arbor, Michigan* 48104 (P50 DE 02731-130021)

In this proposal we will test the hypothesis that specific types of bacteria or certain proportional increases of these specific bacteria are associated with or etiologically responsible for the various forms of periodontal disease. We will do this by identifying patients or teeth which exhibit one of the following clinical conditions: gingivitis, acute necrotizing ulcerative gingivitis, pregnancy gingivitis and periodontitis in young and old individuals. Plaque will be removed from discrete sites of known clinical status, cultured under a system of complete anaerobiosis, and the predominant flora characterized to genus and species level, where possible, using procedures developed during the past term of the grant proposal. If specific bacteria are associated with periodontal disease, then there exists the possibility that if this pathologic flora can be eliminated or suppressed, a nondisease-associated plaque will reestablish. We will treat individuals diagnosed as having periodontal disease with antimicrobial agents alone or in conjunction with mechanical debridement procedures. Antimicrobial treatment will be of a short duration, i.e., 1 to 2 weeks and will include agents such as Flagyl R either alone or in combination with mechanical treatment. The flora changes before and after drug treatment will be monitored and compared to a suitable placebo treatment. The bacterial flora associated with periodontal disease in diabetics will also be studied. In addition, basic studies on the isolation of oral spirochetes, and the ecology of the oral gliding bacteria will be performed. We will collaborate with Drs. Lopatin and Ramfjord in examining for important periodontopathic organisms which may be encountered in their studies.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $311,577

2.0140, HOST RESPONSE IN PERIODONTAL DISEASE (HUMAN)

R.J. Genco, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (P50 DE 04898-030002)

SPECIFIC AIMS: Several specific approaches are defined to elucidate participation of the host's immunologic responses to oral microbial products in human periodontal diseases. A. To determine the relationship of serum antibodies to a 'common plaque' antigen produced by Actinomyces viscosus, Leptotrichia buccalis and Bacteroides melaninogenicus in various forms of IJP patients such as adherence, contact angle, random mobility, bacteriocidal activity, and nitroblue tetrazolium (NBT) reduction. (5) Measuring phagocytosis and bacteriocidal activity of local neutrophils from gingival fluid of patients with IJP. (6) Evaluating neutrophil functions in other forms of periodontal disease such as periodontitis and ANUG.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $124,224

2.0141, IGG FC-RECEPTOR ON ORAL STREPTOCOCCI

H.F. Mengoli, West Virginia University, School of Medicine, Dept. of Microbiology, *Morgantown, West Virginia* 26506 (R01 DE 04631-02)

The objective of this proposal is the study of the non-immune interaction of an oral streptococcal cell wall surface component with the Fc region of normal mammalian IgG. The primary function of this study will then be the evaluation of this interaction as a means by which streptococci potentiate inflammatory disease processes within the oral cavity. The study of this interaction will be approached in the following manner; 1) The prevalence and expression of the IgC(Fc) reactive component by four oral streptococcal species (S. sanguis, S. Salivarius, S. mitis and S. mutans) will be determined; 2) The streptococcal IgG (Fc) reactive component will be extracted from the bacterial surface, isolated and prepared in purified form; 3) The purified IgG (Fc) reactive streptococcal component will be reacted with mammalian IgG and complement fixation and activation assessed in vitro; 4) The inflammatory potential of the IgG (Fc) reactive streptococcal component and IgG will be assessed in vivo by the induction of localized Arthus type reactive and experimental induction of periodontal disease; 5) The functional significance of bacterial bound IgG (Fc) reactive streptococcal component as a suppressor of immune clearance will be evaluated.

This study is designed to investigate the potential role of the IgG (Fc) reactive component in the establishment and development of oral inflammation. As such, the proposal will clearly determine the inflammation potential of the interaction of the purified bacterial component with mammalian IgG and complement, but also the proposal will investigate a mechanism (mediated by streptococcal IgG (Fc) reactive component) by which the streptococcus can establish itself in the ecological niche of the mouth. Major emphasis will be placed on the interaction of this bacterial component with host immune constituents and the use of these constituents to the selective advantage of the invading bacterium.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,

National Inst. of Dental
Research $36,820

2.0142, PERIODONTAL DISEASES - B CELLS ACTIVATED BY MITOGENS

J.A. Clagett, University of Washington, School of Dentistry, Dept. of Periodontics, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (R01 DE 04887-02)

Periodontal disease is the most common cause of tooth loss in the adult population in the U.S. In advanced periodontal lesions, plasma cells are the predominant cell type observed yet the origin and the role of these cells in the pathogenesis of the disease remains largely unknown. Although there is evidence that specific immunity to bacterial antigens may be important, recent data from our laboratory suggest that nonspecific polyclonal activation of host B-cells by substances from the dental plaque bacterium, Actinomyces viscosus (AVIS) may play an important role in the recruitment, maturation and differentiation of B-cells into plasma cells in periodontal lesions. Different polyclonal B-cell activators (PBAs) are believed to trigger distinct maturational subclasses of B-cells to synthesize DNA and/or hastened maturation depending on the activating substances. Thus, selected PBAs such as dextran sulfate (DS), lipopolysaccharide (LPS) from gram-negative bacteria and AVIS can serve as useful functional markers. As a partial explanation for the appearance of plasma cells in periodontal lesions, one possibility is that within a host B-cell subpopulations are selectively recruited, activated and driven to maturity. The aim of the proposed studies is to compare the PBA responses of B-cells in two organs; the bone marrow, in which immature B-cells predominate and the spleen, the B-cell populations of which is composed of largely mature B-cells. In both organs short-lived and long-lived mature and immature B-cells will be selectively tagged with 3H-TdR. Therefore, we can visualize directly the results of stimulation by DS, LPS and AVIS on any given subpopulation of B-cells. Blastogenesis, DNA synthesis and the expression of cytoplasmic and cell surface immunoglobulin will be used as indices of cell activation or maturation. Knowledge of the state of maturation, lifespan, and differential activation by selected PBAs may provide the rationale for the development of new therapeutic approaches in the control and treatment of periodontal and other chronic inflammatory diseases.

BIBLIOGRAPHIC REFERENCES: J.A. Clagett and R.C. Page. Insoluble immune complexes and periodontal diseases in man and the dog. Arch. Oral Biol. 23: 153-165, 1978. J.A. Clagett and L.D. Engel. Polyclonal activation: A form of primitive immunity and its possible role in chronic inflammatory diseases. Develop. and Comp. Immunol. 2: 235-242, 1978.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $49,764

2.0143, REGULATION OF CUTANEOUS BASOPHIL HYPERSENSITIVITY

W.W. Bullock, Oregon State Higher Education System, University of Oregon Health Sciences Center, School of Dentistry, Dept. of Microbiology, *611 S.W. Campus Dr., Portland, Oregon* 97201 (R01 DE 05365-02)

This work is designed to understand how the presence of helper and suppressor thymic-derived cells (T-cells) effect the delayed-type-hypersensitivity (DTH) skin reaction. This study uses azobenezene-arsonate-N-chloroacetyl-tyrosine (ABA-T) as the determinant being recognized by the regulatory T-cells. The ABA-T determinant is covalently bonded to human-gamma-globulin (HGG). This coupling permits regulatory T-cells, specific for ABA-T, to control the DTH skin response to HGG. The regulation is being studied in vivo and in vitro.

BIBLIOGRAPHIC REFERENCES: Wesley W. Bullock, 1978. ABA-T Determinant Regulation of Delayed Hypersensitivity. Immunological Reviews, 39:1-35. Wesley W. Bullock, 1979. Suppression of Delayed Hypersensitivity to Arsanilate-Tyrosine in Adult and Juvenile rats: Freund's complete adjuvant (CFA) or New Carrier Determinants Can Break Tolerance in Juvenile But Not in Adult Rats. Fed. Proc., 38:1022.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $43,515

2.0144, BLOC TRAVEL FOR N.I.D.R. SUPPORTED INVESTIGATIONS

D.B. Green, American Assn. for Dental Research, *734 15th St. N.W., Room 809, Washington, District of Columbia* 20005 (R13 DE 05614-01)

The objective of this proposal is to provide opportunity for dental investigators of the United States to participate in the 58th General Meeting of the International Association for Dental Research in Osaka, Japan. The specific aims of the proposal are to permit the results of N.I.D.R. supported research to be disseminated expeditiously to a world-wide scientific audience, and to provide means by which N.I.D.R. supported researchers may obtain information on the most current dental investigations being conducted outside the United States. A process has been developed to provide a systematic and fair way for the disbursement of travel funds to individual N.I.D.R. grantees. Abstracts of papers prepared for presentation at the Osaka meeting will be reviewed by the Program Committee of the American Association for Dental Research. Selected papers will be forwarded to the I.A.D.R. Program Committee for inclusion in the Osaka meeting. The decisions of the A.A.D.R. Program Committee will assign high priority to: (1) originality of research design, 2) innovations of technique, and 3) the scientific merit, as appraised by the Travel Grants Committee.

The proposed funding is for travel only for approximately 60-65 scientists who are engaged in N.I.D.R. supported research. Assignment of travel funds will be on the basis that the research to be reported is closely related to that being funded by the N.I.D.R. Travel will be from New York to Japan and return, and travel by United States carriers will be required. Funding should not exceed $1,200.00 for any individual involved and will not be less than $700.00. Costs for domestic travel will vary since each presenter must travel to an assembly point (Los Angeles) on the west coast from a variety of cities in the United States.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $75,104

2.0145, COMPLEMENT ACTIVATION AND INFLAMMATION

A.L. Sandberg, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Humoral Immunity Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00061-06 LMI)

The mechanisms by which the complement system regulates the metabolism of connective tissue continue to be investigated. In organ cultures of fetal rat bones, complement activation initiated by antibodies reactive with cell surface antigens results in the enhanced synthesis of prostaglandins which, in turn, causes resorption of the bone. A cell similar to a monocyte may be responsible for the elevated levels of prostaglandins found in these cultures since complement activation by immunoglobulins stimulates prostaglandin production by macrophages in culture. Immunoglobulin fragments which are incapable of directly activating these cells but which activate the alternative complement pathway are effective in this regard. Following interaction of the components of the complement system with macrophage membranes, enhanced incorporation of prostaglandin precursors into prostaglandins occurs. These studies demonstrate that both steroid as well as non-steroid inhibitors of prostaglandin biosynthesis abrogate this response. Complement activation also inhibits the growth of bone in organ cultures of calvaria. Although prostaglandin production is stimulated in these cultures, this event is unrelated to bone growth since indomethacin inhibits prostaglandin production but does not restore bone growth.

BIBLIOGRAPHIC REFERENCES: Wahl, L. M., Olsen, C. E., Wahl, S. M., McCarthy, J. B., Sandberg, A. L. and Mergenhagen, S. E. Prostaglandin and cAMP regulation of macrophage involvement in connective tissue destruction. N. Y. Acad. Sci. 1979. In press. McCarthy, J. B., Wahl, S. M., Rees, J., Olsen, C. E., Sandberg, A. L. and Wahl, L. M. Regulation of macrophage collagenase production by 3'-5' cyclic adenosine monophosphate. J. Immunol. 1979. In press.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $106,231

2.0146, IMMUNOLOGICAL CONTROL OF CONNECTIVE TISSUE METABOLISM

L.M. Wahl, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Humoral Immunity Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00216-03 LMI)

The purpose of this project is to study the role of the immune system in connective tissue metabolism. We have demonstrated that the prostaglandins control the production of collagenase by endotoxin and lymphokine activated macrophages by regulating the intracellular levels of cyclic nucleotides (cAMP). Additionally, drugs, such as Beta adrenergic stiumlators, dibutyryl cAMP and phosphodiesterase inhibitors, which directly effect cAMP metabolism have been shown to modulate both prostaglandin and collagenase production of endotoxin activated macrophages. High concentration of these cAMP enhancing agents significantly inhibit the production of prostaglandin and collagenase whereas both are stimulated by lower concentrations of these drugs. Studies involving the role of the immune system in bone resorption have revealed that macrophages from an osteopetrotic rat (toothless rat) model are defective in the production of prostaglandins and in the production of suppressors of lymphocyte proliferation. The lower production of prostaglandins by macrophages from the osteopetrotic rats may in part be one of causes for the hyperproliferation of lymphocytes in the animals since prostaglandins are known to suppress lymphocyte proliferation.

BIBLIOGRAPHIC REFERENCES: Mergenhagen, S. E., Rosenstreich, D. L., McGhee, J. R., and Wahl, L. M. Potential role of lymphorecticular cells in the Host Response to Endotoxin. Immunology, Ed. Gergely, Medgyesi and Hollan, 1978. pp. 431-447. Wahl, S. M., Wahl, L. M., McCarthy, J. B., Chedid, L. and Mergenhagen, S. E. Macrophage activation of mycobacterial water soluble compounds and synthetic muramyl dipeptide. J. Immunol. 122: 2226-2231, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$100,039

2.0147, INCIDENCE OF RADICULAR CYSTS IN ATTACHED PERIAPICAL TISSUE FOLLOWING ROUTINE DENTAL EXTRACTION

J.H. Simon, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Endodontic Section, *5901 E. 7th St., Long Beach, California* 90822 (600-004-P)

This study investigates, by way of serial sections, the relationship between tooth apex, root canal (and contained necrotic material) and periapical pathoses. The emphasis is on cystic pathogenesis versus apical epithelial proliferation. We hope that the distinction between these 'true cysts and apical pockets' may lead to change in current treatment philosophy. The investigation is nearly one-half completed. We have obtained 34 specimens which fit the criteria for the study. It was necessary to obtain and submit approximately 40 extracted teeth also containing an attached periapical lesion. Of these 40 teeth, 6 were lost to the study due to difficulties in processing and sectioning. Thus far, all the cases have been obtained from the Oral Surgery Service at the Long Beach Naval Station and we hope to get more teeth as time goes by. We would like to study 50 cases. The completed cases have been serially sectioned and stained. Each case has been stained with Hemotoxin and Eosin and Brown/Bren since we will be looking not only for periapical pathosis but also a relationship between the lesion, the tooth and the extent of bacterial involvement in the periapical tissues. To date, 25 cases have been studied. While it is too early to draw conclusions, it appears that the incidence of true cysts may be about 5%. This would be contrary to the prevalent % of 42 and tend to question the belief that cysts heal with nonsurgical endodontic therapy.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0148, BEHAVIOUR OF ORAL MUCOSA IN ORGAN CULTURE AND ITS REACTION TO PRODUCTS OF THE INFLAMMATORY RESPONSE

A.E. Miles, University of London, London Hospital Medical College, Dept. of Oral Pathology, *Turner St., London E1 2AD, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$23,461

2.0149, CYTOLOGICAL STUDY OF THE DESMODONTE

J.P. Proust, Universite dAix Marseille, Faculte de Chirurgie Dentaire, Dept. of Biology & Fundamental Materials, *Charles Livon Blvd., Jardin Emile Duclaux, 13007 Marseille, France*

This project is more particularly concerned with the study, with the aid of the electronic microscope, of the cells involved in the inflammatory processes affecting the desmodonte.

SUPPORTED BY

Universite dAix Marseille	funds n.a.

PATHOLOGY - TISSUE DESTRUCTION & HEALING

2.0150, ULTRASTRUCTURE AND PHYSIOLOGY OF ORAL MUCOSA

G. Szabo, Harvard University, Boston Campus, School of Dentistry, Dept. of Oral Biology, *188 Longwood Ave., Boston, Massachusetts* 02115 (R01 AM 20669-17)

In the coming year, we will continue our studies on the effect of ultraviolet light on the epidermal melanocyte and cultured retinal pigment epithelial cells. We will devise a system by which psoralen together with UVL can be used in our organ culture and cell culture systems, in order to elucidate the mode of action and synthesis of tyrosinase, on the activation of tyrosinase within the melanosomes, and on the melanization of melanosomes. In the combined epidermal keratinocyte and melanocyte cultures, we will study the possible influence of psoralen and UVL on melanosome transfer and melanocyte-keratinocyte interactions. In this same culture system, we will study melanocyte-keratinocyte interactions at the electron microscopic level using freeze-fracture techniques.

We will continue our in vivo studies on melanocyte-keratinocyte interactions in the guinea pig, with special reference to the effect of psoralen and UVL. We also plan to make use of a very interesting genetic variant in the mouse, the C57 dilute black, in which melanosome transfer seems to be impeded. We have found that in this system ultraviolet irradiation increases melanocyte number but does not increase, to any great degree, melanosome transfer. Since there are some indications that similar disorders in man may be associated with severe immunological deficiencies, a study of this system may be of great importance in the investigation of cell-to-cell interactions.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Arthritis
Metabolism & Digestive
Diseases $135,257

2.0151, NUTRITION ON THE EPITHELIUM OF ORAL MUCOUS MEMBRANES

C. Enwonwu, University of Washington, School of Dentistry, Dept. of Oral Biology, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (N01DE42442 (CONTRACT))

OBJECTIVES AND WORK SCOPE: The objective of this research project is to determine the influence of protein, calorie, and vitamin deficiencies on oral mucous membranes in experimental animal model systems. Comparisons will be made between undernourished animals and those maintained on normal diets to determine the separate effects of chronic, progressive protein, calorie and vitamin deficiency on the health of the oral tissues. Tests conducted on the oral tissues of 3-4 year old Rhesus monkeys will determine (1) cell turnover rates, (2) level of keratinization in keratinizing epithelium, (3) degree of alteration of metabolic processes (enzyme systems or protein synthesis), and (4) studies of basement membranes of the various epithelial linings.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $68,020

2.0152, THROMBIN AND PROTHROMBIN

R.L. Lundblad, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Periodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130190)

The factors governing the specificity of thrombin, a pivotal enzyme in normal blood coagulation will be elucidated by a multi-faceted approach based on solution chemistry including specific chemical modification and limited proteolysis. Specifically, the unique structural characteristics of thrombin important for the interaction of this enzyme with fibrinogen, heparin, platelets and antithrombin III will be identified in order to provide greater insight into the relationships between chemical structure and function in primary and secondary hemostasis. The structure of prothrombin, the precursor of thrombin, will also be studied by the use of the above solution chemistry techniques to delineate features of the molecule critical for normal activation.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $96,213

2.0153, A STUDY OF EPITHELIAL-CONNECTIVE INTERACTIONS WITH SPECIAL EMPHASIS ON THE BIOSYNTHESIS OF THE BASAL LAMINA

D.K. MacCallum, University of Michigan, Ann Arbor Campus, School of Dentistry, *Ann Arbor, Michigan* 48104 (P50 DE 02731-130032)

This project is attempting to establish two in vitro model systems for the purpose of studying synthesis of the basal lamina and the effect of different substrata on the induction of laminar synthesis. One system utilizes cultured corneal endothelial cells. These cells synthesize and organize a conspicuous basal lamina in culture. Using this system, synthesis and transport of laminar subunits will be studied using combined ultrastructural and biochemical methods. The in vitro-formed membrane will be analyzed for similarities with the native membrane. The second system utilizes cultured stratified squamous epithelium of rodent oral origin. These epithelial cells, which can be subcultured, will be plated on substrata including various collagen types, collagenaproteoglycan mixtures, and a basal lamina (in vitro Descemet's membrane). The effect of these substrata in inducing secretion and organization of epithelial basal cells will be studied using combined ultrastructural and biochemical methods. Static and migrating lingual epithelium in organ culture will also be studied by autoradiography and electronmicroscopy to determine differences in rates of synthesis and factors affecting organization of exported laminar subunits.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$97,885

2.0154, INTERACTIONS OF CELLS WITH TOOTH SURFACES

M.E. Neiders, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Pathology, *3435 Main St., Buffalo, New York* 14214 (R01 DE 03689-03)

It is proposed to study cell detachment mediated by cellular and bacterial products found in the gingival sulcus using an in vitro assay and relating these findings to detachment of cells from each other and tooth surfaces in the pathogenesis of periodontal disease. The assay consists of incubating adherent cells with a test agent and determining the percent of detachment in comparison with controls after application of a known and reproducible shearing force. Cell supernatants from stimulated lymphocytes, lysates of polymorphonuclear leukocytes and dental plaque have been shown to enhance cell detachment. Further studies will characterize the components that produce cell detachment in cell supernatants following separation by ion exchange and gel chromatography. Established lymphoid cell lines will be assayed for ability to detach cells in the hope to be used as prototypes for detachment-enhancing activity seen with normal stimulated mononuclear cells. The mechanisms for cell detachment will be investigated. Cell detachment by plaque will be related to the degree of disease severity in the individual from whom the plaque was obtained.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$16,801

2.0155, HEALING AND FATE OF FREE GINGIVAL GRAFTS

R.G. Caffesse, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *2215 Fuller Rd., Ann Arbor, Michigan* 48105 (506-001-F)

Conclusions of the manuscript 'Healing of Free Gingival Grafts With and Without Periosteum. Radioautographic Evaluation' in press in the Journal of Periodontology. Within the limits of this study, the following conclusions can be drawn: 1. The total rate of cell proliferation after a free gingival graft procedure is similar whether on periosteum or on bone. 2. Proliferation from the surrounding tissues will be sufficient to warrant the success of the graft. 3. The presence of the periosteum in the bed will provide a source for initial repair at the interface. 4. Remnants from deep rete pegs in the graft will contribute to its reepithelization. 5. Delayed remodeling is expected when grafts are placed on bone. This affects mainly the newly formed periosteum.

The paper 'The Role of Sulcular Environment in Controlling Epithelial Keratinization' has been published in the Journal of Periodontology, 50:1, 1979.

Further studies are being carried out related to the effect of antibacterial therapy in the keratinizing potential of the sulcular epithelium. They will result in several publications in the future.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0156, THE LANGERHANS CELL - RETICULOEPITHELIAL DROP OF THE GINGIVAL MUCOSA

R.S. Gilman, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Leavenworth, Kansas* 66048 (686-001-I)

Using light microscopy and histochemical staining techniques it will be possible to demonstrate selective uptake of contact allergens by the Langerhans cells of human gingival epithelium. Fresh specimens of clinically normal human gingiva will be stained with two aldehydes; formaldehyde and gluteraldehyde, an amine; paraphenylene diamine, two metals; gold and chromium and two stains; ATPase and dopa (dihydroxysphenylalanine). It is posterlated that the Langerhans cells, site of hapten binding and (thus) antigen formation, form a reticulo epithelial system that may clear the gingiva of foreign substances.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0157, THE USE OF INTRAORAL PORCINE HETEROGRAFTS FOR GINGIVAL REPAIR

T.N. Sims, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-006-F)

This study accessed the utilization of porcine heterografts material to split thickness connective tissue beds as an alternative method to free gingival grafting for increasing the zone of attached gingiva, in 6 veteran male patients. In the patients studied the porcine material served as a bandage to allow re-epithelialization of the connective tissue wound. Healing was rapid and uneventful. However, healing was markedly decreased from conventional techniques using autogenous gingival tissue. The porcine material did provide a significant advantage over nondressed granulation and re-epithelialization in promoting healing and decreasing both recipient and donor site patient pain. There was a degree of unpredictability regarding the amount of attached gingival tissue in the final healed surgical site. Because of this variability investigators felt further study was not warranted.

SUPPORTED BY

U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

2.0158, MORPHOMETRIC AND STERIOLOGICAL ANALYSIS OF NORMAL AND PATHOLOGICAL HUMAN ORAL MUCOSA

C.J. Smith, University of Sheffield, Dept. of Oral Pathology, *Mappin St., Sheffield S3 7RE, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council $29,884

2.0159, IMMUNOFLUORESCENT IDENTIFICATION OF BASEMENT MEMBRANES

G. Wick, Leopold Franzens Universitat Innsbruck, *Innrain 52, 2 6 Universitatsstrasse, A6020 Innsbruck, Austria* (N01DE82412 (CONTRACT))

OBJECTIVE: Perform indirect immunofluorescent localization of reactive structures with specific antibodies, utilizing antibodies against: purified tumor basement membrane collagen; type I procollagen; type III procollagen; and fibrinogen or some other noncollagenous, nonconnective tissue protein.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

2.0160, BIOCHEMISTRY OF CROSS-LINKING OF COLLAGEN

G.L. Mechanic, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Pedodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130125)

The overall objectives and long term goals for the proposed work are (1) to determine if collagen aldehydes and their time-dependent intermediate Schiff base intermolecular crosslinks bear any relationship to the biochemical phenomena that cause intercellular matrix collagen fibrils to become increasingly more insoluble as maturation and aging of an organism ensues and progresses; (2) to be able to explain the chemical phenomena that cause the intercellular macromolecular collagen matrix to become insoluble as an animal ages; (3) to ascertain the mechanisms, catalytic or otherwise, responsible for the crosslinking and stabilization of the polymolecular matrix of collagen after its self-assembly into a quarternary structure (fibrils); and (4) to determine the biochemical specificities inherent in the collagen molecule's micromolecular structure, that cause specific intra- and intermolecular covalent crosslinks to form in specific extracellular tissues. Insoluble mineralized tissue collagen, soluble collagen of tendon and skin as well as the latter's insoluble counterparts from pre and post-natal animals at various stages of development, maturation and aging, will be aged in vitro. Natural collagen fibrils, not subjected to any extraction procedures, from the same animals will also be used. The collagens will be examined quantitatively for reducible Schiff base and stable ketoimine crosslinks by a variety of chemical methods. After specific cleavage of the collagen, the loci of these crosslinks will be determined by amino acid composition and sequence of homogeneous crosslink peptides. Investigations will also be pursued in quantification of in vivo, and in vitro incubated, reduced Schiff bases as well as nonreducible stable crosslinks that form on maturation and aging of a collagenous tissue.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $76,196

2.0161, BIOCHEMISTRY OF AVIAN OSTEOGENIC OSTEOBLASTOMA - IN VIVO AND IN VITRO STUDIES

G.L. Mechanic, University of North Carolina, Chapel Hill Campus, Dental Research Center, Dept. of Surgery, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130176)

Infection of 12 day-old chick embryos with Myeloblastosis-associated virus-2(osteo). (MAV-2(O)) causes the formation of tumors in long bones. The resulting disease, avian osteogenic osteoblastoma (formerly avian osteopetrosis) involves a change in quantitative collagen crosslinks as well as collagen synthesis in bone collagen from affected birds. In addition, collagen crosslinks and synthesis in chick cells infected in vitro share a similar pattern to that observed for in vivo specimens. The objectives of this study are to examine the molecular biology of collagen produced in diseased birds and MAV-2(O)-infected cells, and to measure rates of collagen and noncollagen protein synthesis as well. Specifically we intend to: 1) examine the patterns of collagen crosslinks of avian osteogenic osteoblastoma, and murine and human osteopetrotic and normal bone and those of uninfected and MAV-2(O)-infected chick embryo cells, 2) to analyze collagen isolated from osteogenic osteoblastoma and normal bone, and from MAV-2(O)-infected and uninfected chick embryo cells for a) collagen chain type; ratio alpha 1/alpha 2 chains, b) CNBr peptide analysis of isolated chains, c) crosslink and amino acid analysis of chains and CNBr peptides. The overall goal of the project is to elucidate the role that collagen plays in the pathogenesis of osteogenic osteoblastoma.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$50,798

2.0162, BIOCHEMISTRY OF COLLAGENOUS AND NONCOLLAGENOUS PROTEINS OF CONNECTIVE TISSUES

W.T. Butler, University of Alabama in Birmingham, School of Dentistry, Dept. of Biocommunication, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130003)

The specific aims of this research are: 1. To determine the covalent structure of type II collagen. a. The elucidation of the complete amino acid sequence of the collagen alpha 1 (II) chain from bovine nasal cartilage. b. To determine the amino acid sequence of portions of the alpha 1 (II) chain of chick sternal cartilage and compare the results to those from bovine alpha 1 (II) chain. c. The location of all the carbohydrate moieties of alpha 1 (II). d. To study in detail the heterogeneity of collagen alpha 1 (II) chains. e. To locate the intermolecular cross-links of the alpha 1 (II) chain of chick sternal cartilage and to specify the hydroxylysyl groups involved in formation of these cross-links. 2. To compare all available sequence data for the collagen alpha 1 (I), alpha 2, alpha 1 (II) and alpha 1 (III) chains in order to gain insights into their relationships and the groups preserved for intermolecular interactions during fibrillogenesis. 3. To determine the exact locations of cross-links in dentin collagen.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$138,774

2.0163, CHEMISTRY AND MOLECULAR BIOLOGY OF THE CONNECTIVE TISSUE PROTEIN, COLLAGEN

E.J. Miller, University of Alabama in Birmingham, School of Dentistry, Dept. of Biochemistry, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130019)

OBJECTIVES: 1. Discovery and elucidation of the biochemical features of the genetically-distinct collagens elaborated in the connective tissue matrices and basement membranes of mammalian organisms. 2. Determination of the manner in which selective use of the structural genes for collagen synthesis is controlled and utilized in normal growth and development as well as in hereditary and acquired diseases of connective tissues.

No major shifts in direction or emphasis of the current research effort are contemplated at this time. However, current indications are that we may be able to develop a cell culture system producing unusual quantities of the basement membrane collagens which will considerably facilitate studies on the biosynthesis of these compounds. Hence, in future years, as the chemical properties of the proteins of interest are elucidated, more emphasis on biosynthetic studies is anticipated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$260,494

2.0164. MATRIX COMPONENT INTERACTIONS IN CALCIFIED TISSUES

A. Veis, Northwestern University, Chicago Campus, School of Dentistry, Dept. of Oral Biology, *Chicago, Illinois* 60611 (R01 DE 01374-19)

The mineralized tissues are comprised from an ordered organic matrix, principally collagen fibers in bone and dentin, in which mineral crystals are deposited. There is a clear relationship between the structure of the matrix and the pattern of deposition of the mineral. The organic matrix components are laid down first, as the initial stage of normal bone and dentin calcification. The objective of our program is to understand the factors, at the molecular mechanistic level, which lead to this orderly deposition of mineral within the matrix. It appears that non-collagenous components of the matrix, phosphophoryns in dentin, interact with collagen at the mineralization front. Because of their high calcium ion affinity, the phosphophoryns, we postulate, fix the first layer of calcium ions upon which further crystal growth can occur. Present studies deal with: 1) the properties of the phosphophoryns; 2) the biosynthesis and secretory pathway of the phosphophoryn; 3) the nature of the interaction between phosphophoryn and collagen at the mineralization front, and 4) the nature of the analogous phosphophoryns (or other acidic proteins) in bone.

BIBLIOGRAPHIC REFERENCES: Phosphophoryns - Major Noncollagenous Proteins of Rat Incisor Dentin. M.T. Dimuzio and A. Veis, Calcified Tissue Research 25, 169-178 (1978). The Biosynthesis of Phosphophoryns and Dentin Collagen in the Continuously Erupting Rat Incisor. M.T. Dimuzio and A. Veis, J. Biol. Chem. (1978), in press.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $66,231

2.0165, THE DEVELOPMENTAL BIOLOGY OF CALCIFIED TISSUES

E.P. Katz, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Oral Biology, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 02953-10)

The extracellular matrices of calcified tissues contain macromolecules which spatially and temporally regulate mineralization and osteogenesis. The long term objective of this project is to elucidate the regulatory properties of these macromolecules in terms of their structure and physical-chemical properties. Studies will be made of the disposition, reactivity and energetics of the electrostatic side chains in bone, dentine and skin matrices. Physical-chemical modification methods will be used.

BIBLIOGRAPHIC REFERENCES: On the Calcium Binding Sites of the Phosphoproteins of Dentine. S.T. Li and E.P. Katz. J. Dent. Res. 57: 56 (1978) (abstract). An Electrostatic Model for Collagen Fibrils: The Interaction of Reconstituted Collagen with H2PO4 and HPO4-2. S.T. Li and E.P. Katz. Proc. Biophysical Soc. 21: 39a (1978) (abstract).

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $59,709

2.0166, CONNECTIVE TISSUE OF PERIODONTIUM COLLAGEN MATURATION

R.C. Page, University of Washington, School of Medicine, Dept. of Pathology, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (R01 DE 03301-09)

Periodontal disease is the most common cause of tooth loss. The disease is caused by interaction of microorganisms with host defense mechanisms resulting in damage to the connective tissues and bone. Similar connective tissue alterations are an important component of many chronic diseases. The mechanisms underlying alterations of this type have not been elucidated. We propose to continue our analysis of normal and diseased connective tissue matrix components and to learn what role fibroblasts play in the pathologic alterations. We will study the quantity, location and distribution of alpha-I trimer collagen which is present in diseased gingiva and is made by cells from this tissue maintained in vitro. This collagen will be purified and characterized with regard to digestability with collagenase and other enzymes, ability to undergo crosslinking with lysyl oxidase and capacity to form fibrils. In addition a group of noncollagenous proteins found in normal dog gingiva but not in diseased dog gingiva will be extracted and purified. The relationship between fibroblast function and pathologic alteration will be investigated as follows. We propose that fibroblast activities are regulated at least in part by the interaction of cell surface binding sites with ligands present in the extracellular environment. We will assess the importance of two such ligands which are already known to affect fibroblast functions. These are prostaglandin and the C1 component of complement. The presence, density and affinity of cell-surface binding sites for prostaglandin will be determined. Cell movement will be measured by cinematography, cell growth by DNA labeling and cell counting, and synthetic activity by radiolabeling and chromatographic techniques. Successful completion of the project will reveal how fibroblasts participate in the pathologic alterations in numerous diseases and may lead to new or improved methods of intervention or prevention.

BIBLIOGRAPHIC REFERENCES: Page, R.C., Davies, P. and Allison, A.C. The macrophage as a secretory cell. Int. Rev. Cytol. 52:119-157, 1978. Engel, D., Schroeder, H.E. and Page, R.C. Morphologic features and functional properties of human fibroblasts exposed to Actinomyces viscosus substances, Infec. & Immun. 19:287-295, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$125,601

2.0167, THE MOLECULAR NATURE OF GINGIVAL AND MUCOSAL COLLAGEN

M.L. Schneir, University of Southern California, School of Dentistry, Dept. of Basic Sciences, *3551 University Ave., Los Angeles, California* 90007 (R01 DE 03318-08)

We will be investigating the effect of streptozotocin-induced diabetes on collagen synthesis and degradation in rat gingiva and other representative connective tissues. Simultaneously, we will examine the rate of synthesis and degradation in tissues of untreated rats, particularly, gingiva. The premise underlying these studies is that the critical metabolic lesion in connective tissues caused by diabetes is an effect on collagen metabolism.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$85,712

2.0168, GINGIVAL COLLAGEN METABOLISM IN HEALTH AND DISEASE

L.M. Golub, State University of New York, Health Science Center at Stony Brook, School of Dentistry, Dept. of Oral Biology & Pathology, *Stony Brook, New York* 11790 (R01 DE 03987-05)

Collagen, the major structural protein of the soft and hard periodontal tissues, is disorganized and destroyed during periodontal disease. The objectives of this study are to study the effects of inflammation and diabetes (a relatively common systemic factor that accelerates periodontal breakdown) on gingival collagen metabolism in rats and humans. More specifically, the animal studies will examine diabetic alterations in (1) gingival collagen biosynthesis, including prolyl and lysyl hydroxylase activity and the formation of H3-hydroxyproline in vivo; (2) the relative amounts of type I and type III collagens in gingiva; (3) gingival collagen maturation, including lysyloxidase activity and the solubility of H3-hydroxyproline labeled collagen formed in vivo. In addition, germ-free rats will be made diabetic to determine whether the diabetes-induced changes in gingival collagen metabolism are a direct effect, mediated by alterations in tissue metabolism, or an indirect effect, resulting from an altered oral microflora. Gingival tissue from systemically-normal and diabetic human subjects (removed during periodontal surgery for therapeutic reasons) will be analyzed for soluble and insoluble collagen content; other samples will be cultured to examine collagen turnover and collagenase activity in vitro. Gingival fluid collagenase activity will be monitored in these subjects, before and at various times after surgery and will be correlated to collagen changes in the adjacent gingival tissues.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$93,144

2.0169, GINGIVAL MATRIX PROTEINS AND PERIODONTAL DISEASE

M.K. Dabbous, University of Tennessee, Center for the Health Sciences, School of Basic Medical Sciences, Dept. of Biochemistry, *800 Madison Ave., Memphis, Tennessee* 38163 (R01 DE 04125-04)

Biochemical characterization of gingival matrix proteins was initiated in our laboratory to establish base line information on the nature of the alterations accompanying inflamatory processes, thereby, defining the role of the intercellular macromolecules in periodontal disease. Detailed structural studies at the molecular level of the collagenous and noncollagenous components of gingivia from normal and diseased tissues are in progress to establish the biochemical nature of these components and their physiological role in the maintenance of gingival tissue.

Since the heterogeneity of gingival collagen has been established in the present phase of the project, it is now essential to characterize the new types of tropocollagen subunit alpha chains and to determine their significance for normal gingival tissue function. The question of modulation in the biosynthetic activity of cells from these tissues will be examined in order to understand the factors which may influence gene expression during inflamatory disease.

Our preliminary data suggested that the noncollagenous moiety which appeared to be firmly associated with the collagenous component, possibly covalently, showed significant change in composition in the diseased tissue.

A corelation of the structural alterations in gingival connective tissue macromolecules with histological and clinical manifestations of peridontal disease will provide more information on the molecular basis and etiology of the disease. Physiocohemical studies using cyanogen bromide cleavage, limited proteolysis, electrophoretic separation, peptide isolation and purification and amino acid and carbohydrate analyses will be used for further biochemical characterization of the tissue components.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$47,775

2.0170, PEPTIDES FROM DENTAL AND OSSEOUS COLLAGENS

R.W. Wyckoff, University of Arizona, School of Liberal Arts, Dept. of Physics, *Tucson, Arizona* 85721 (R01 DE 04635-02)

The work covered by this Grant develops and tests physical techniques that can give information about the microstructure and microcomposition of fresh and fossil teeth and other hard tissues. The methods currently being used to investigate microstructure include various types of optical micrography, electron microscopy, and the scanning electron microscopy of surfaces and section. Microcomposition is being studied by X-ray spectrocopy, electron probe analysis and by the quantitative chromatography of isolated organic constituents.

BIBLIOGRAPHIC REFERENCES: Ralph W.G. Wyckoff and Franklin D. Davidson, 'Pleistocene and Dinosaur Gelatins,' Comp. Biochem. Physiol., 55B, 95-97 (1976).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0171, COLLAGEN SYNTHESIS IN DILANTIN GINGIVAL HYPERPLASIA

K.B. Benveniste, University of Maryland, Baltimore Professional Schools, School of Dentistry, *66 W. Baltimore St., Baltimore, Maryland* 21201 (R01 DE 04776-01)

The influence of Dilantin on collagen biosynthesis in gingival fibroblasts will be studied. Fibroblast cell lines will be established from patients receiving Dilantin who are either responders or nonresponders and from normal controls. The increased rate of collagen synthesis observed by other investigators will be compared to overall protein synthesis and quantitated. Further experiments will be directed toward determining whether an increase in transcription or translation is responsible for the increased rate of collagen synthesis. RNA will be labeled in culture and the half-life of the total messenger and the collagen mRNA populations will be determined. In addition, mRNA will be extracted from the fibroblasts and functional collagen mRNA quantitated by translation in a heterologous cell-free protein synthesizing system.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0172, COLLAGEN SYNTHESIS IN DILANTIN GINGIVAL HYPERPLASIA

K.B. Benveniste, Northwestern University, Chicago Campus, School of Dentistry, Dept. of Oral Biology, *Chicago, Illinois* 60611 (R01 DE 05547-02)

The influence of Dilantin on collagen biosynthesis in gingival fibroblasts will be studied. Fibroblast cell lines will be established from patients receiving Dilantin who are either responders or nonresponders and from normal controls. The increased rate of collagen synthesis observed by other investigators will be compared to overall protein synthesis and quantitated. Further experiments will be directed toward determining whether an increase in transcription or translation is responsible for the increased rate of collagen synthesis. RNA will be labeled in culture and the half-life of the total messenger and the collagen mRNA populations will be determined. In addition, mRNA will be extracted from the fibroblasts and functional collagen mRNA quantitated by translation in a heterologous cell-free protein synthesizing system.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,

National Inst. of Health,
National Inst. of Dental
Research $54,960

2.0173, ORAL MANIFESTATIONS OF PHENYTOIN THERAPY

T.M. Hassell, University of North Carolina, Chapel Hill Campus, School of Dentistry, *Chapel Hill, North Carolina* 27514 (R13 DE 05433-01)

The purpose of this international symposium on oral manifestations of phenytoin therapy is to bring together, essentially for the first time, basic science and clinical researchers who have demonstrated expertise in approaching the various oro-facio-dental problems which result from long-term phenytoin ingestion. Fourteen invited speakers will present their most recent research in collagen biochemistry, immunology, histopathology, pathophysiology, teratology, periodontology, pharmacology, epidemiology and related fields. A panel discussion will permit direct interaction among experts in various disciplines.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $9,528

2.0174, GINGIVAL COLLAGEN METABOLISM IN HEALTH AND DISEASE

M.L. Mailman, University of Texas, Health Science Center at Houston, Dental Branch, *6515 Freeman, Houston, Texas* 77025 (R23 DE 04691-03)

The proposed study is directed toward a comparison of collagen metabolism in healthy and in inflammed gingiva during the course of inflammatory periodontitis. Specifically, collagen synthesis in normal and diseased gingiva will be studied using biochemical probes to determine (1) total content of collagen in gingiva during the progress of the disease; (2) the maturational state of collagen in diseased tissues by comparing the solubility distribution of collagen into salt-soluble, acid-soluble, and insoluble fractions in inflammed and healthy gingiva; and (3) the rate of collagen synthesis relative to total protein synthesis in diseased versus healthy tissues. The characterization studies (01 and 02) will be based on a systematic analysis of the content of hydroxyproline in the tissues and its solubility distribution. The relative rate studies (03) will be performed by labelling gingival tissues in vitro with 3H-proline and digesting the labelled proteins with protease-free bacterial collagenase to separate collagen and non-collagen proteins. Rates of collagen vs non-collagen protein synthesis will be determined from the kinetics of 3H-proline incorporation into each moiety. The relationship between collagen content, collagen solubility, and rate of synthesis during the progress of inflammatory periodontitis will allow an assessment of whether an impairment in collagen synthesis and/or maturation contribute to the loss of collagenous structures during the course of the disease.

BIBLIOGRAPHIC REFERENCES: Mailman, M.L. and Simpson, J. (1978). Production of a collagenase inhibitor by gingival fibroblasts (Abstract). J. Dent. Res. 57A, 264. Simpson, J.W., Mackler, B.F., O'Neill, P.A., Mailman, M.L., Adams, S. and Harris, J. (1978). Collagenase production by human peripheral blood mononuclear cells. (Abstract). J. Dent. Res. 57A, 264.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $36,534

2.0175, MOLECULAR MECHANISMS OF PERIODONTAL DISEASE

M.Z. Hussain, University of California, San Francisco Campus, School of Dentistry, Dept. of Periodontology, *551 Parnassus Ave., San Francisco, California* 94122 (R23 DE 04752-03)

An obvious consequence of periodontal disease is the loss of large amounts of tissue collagen, which in earlier stages of the disease, is related to increased degradation lost in chronic syndromes, may arise from decreased synthesis. Studies using culture of gingival fibroblasts derived from clinically healthy and diseased subjects show a change in the rate of collagen synthesis as well as the types of collagen synthesized. Since the compliment of tRNA in a tissue may be adapted for the synthesis of specific protein and the levels of particular tRNA species seem to regulate the amount of collagen, we plan to study the possible involvement of codon-specific isoaccepting tRNA species related to collagen synthesis. The primary objective of this work is to determine if qualitative or quantitative differences in collagen characteristic tRNA species exist between cultures of gingival fibroblasts derived from healthy and diseased sources. The results of these studies will be compared with those obtained from chondrocytes cultured under conditions in which they produce elevated levels of collagen. The comparative study of this nature therefore, may enable us to obtain basic information on the cellular level which we hope will be useful in explaining the alteration of collagen content in periodontal disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$28,992

2.0176, CHEMISTRY AND BIOSYNTHESIS OF CONNECTIVE TISSUE

G.R. Martin, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00009-18 DB)

For summary: see 7.0005.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$54,970

2.0177, REGULATION OF COLLAGEN BIOSYNTHESIS IN NORMAL AND DISEASED TISSUES

L.M. Paglia, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00025-13 DB)

The purpose of this project is to investigate the regulation of collagen biosynthesis in normal and diseased cells. Here we are concerned with translational control of biosynthesis and posttranslational steps in helix formation.

BIBLIOGRAPHIC REFERENCES: Paglia, L., Wilczek, J., Diaz de Leon, L., Martin, G.R., Horlein, D. and Muller, P.: Inhibition of procollagen cell-free synthesis by amino terminal extension peptides. Biochemistry. In press, 1979. Salomon, D., Paglia, L. and Verbruggen, L.: Hormone dependent growth of a rat chondrosarcoma in vivo. Cancer Research. In press, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$122,031

2.0178, ATTACHMENT OF CELLS TO COLLAGEN

H.K. Kleinman, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00230-03 DB)

The purpose of this project is to study the mechanism of cell attachment to collagenous matrices. Particular attention is directed towards: 1) the attachment properties of various cultured and non-cultured cells and whether cell synthesize or utilize attachment proteins different than fibronectin, 2) the nature of the attachment protein(s) specificity for different collagens and reconstituted collagen and 3) the interaction of adhesion proteins with other molecules and with cells.

BIBLIOGRAPHIC REFERENCES: Silbert, C.K. and Kleinman, H.K.: Studies of cultured human fibroblasts in diabetes mellitus: Changes in heparan sulfate. Diabetes 28: 60-64, 1979. Kleinman, H.K., McGoodwin, E.B., Rennard, S.I. and Martin, G.R.: Preparation of collagen substrates for cell attachment: Effect of collagen concentration and phosphate buffer. Anal. Biochem. 94: 308-312, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$142,196

2.0179, MORPHOGENETIC ROLE OF TISSUE-SPECIFIC PROCOLLAGEN

E.J. Kollar, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Oral Biology, *Farmington Ave., Farmington, Connecticut* 06032 (PCM76-19975)

Research is underway to characterize procollagen isolated from primary cell cultures of cranial neural crest derivatives (embryonic mouse tooth buds, Meckel's Cartilage, and mandibular mesenchyme) and to determine the tissue specificity of the various classes of procallagen. Medium from large-scale cell cultures containing the procollagen is being harvested and the procollagen isolated. The alpha chain composition of procollagen is being determined by CM-celluose chromatography.

The morphogenetic influence of procollagen during histogenesis is being evaluated by supplying procollagens of known alpha chain composition to explants of embryonic mouse tooth germs in which endogenous procollagen synthesis is suppressed by alpha, alpha-dipyride or L-azetidine-2-carboxylic acid.

The deposition and distribution of collagen fibers is being determined by autoradiographic and electron microscopic techniques. The ability of the various procollagens to circumvent the inhibition of endogenous collagen synthesis and to support continued morphogenesis (despite constant presence of the collagen antimetabolites) is being determined from histological evaluation and comparisons with untreated control explants.

SUPPORTED BY

U.S. National Science Foundation, Directorate for Biological Behavioral & Social Sciences, Div. of Physiology Cellular & Molecular Biology	$0

2.0180, LONG TERM EFFECTS OF FLUORIDE INTAKE

L. Singer, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160078)

For summary: see 1.0270.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$24,032

2.0181, METABOLISM OF CONNECTIVE TISSUE PROTEOGLYCANS

L. Roden, University of Alabama in Birmingham, School of Dentistry, Dept. of Biochemistry, *1919 7th Ave. S., Birmingham, Alabama* 35233 (P50 DE 02670-130024)

It is proposed to investigate the biosynthesis of heparin. A major objective is to determine loci of regulation of polymer assembly and to study the structural and functional organization of the enzymatic apparatus required for this process. Besides equipment for synthesis of a protein core, six glycosyltransferases are needed for polysaccharide chain formation, and five other enzymes catalyze a series of modifications which take place after initial assembly of the carbohydrate portion of the molecule. A thorough knowledge of these enzymes is required to understand the biosynthesis of heparin.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$156,144

2.0182, ULTRASTRUCTURE AND BIOSYNTHESIS OF CARTILAGE PROTEOGLYCANS

G.K. Hascall, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Experimental Morphology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00163-03 LBS)

This project uses electron microscopy, histochemistry, and autoradiography to study the biosynthesis of cartilage proteoglycans and their relationship to collagen in cartilage matrix. Current studies include electron microscopy of the Swarm rat chondrosarcoma and cells cultured from it, including the use of tracers to detect sites of uptake in the chondrocytes, and electron microscopy of abnormal cartilage from mice and humans.

BIBLIOGRAPHIC REFERENCES: Faltz, L.L., Reddi, A.H., Hascall, G.K., Martin, D.M., Pita, J., and Hascall, V.C.,: Characteristics of Proteoglycans Extracted from the Swarm Rat Chondrosarcoma with Associative Solvents. J. Biol. Chem. 254, 1375-1380, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$45,635

2.0183, AUTOGENOUS DENTIN GRAFTS FOR PERIODONTAL DEFECTS

T.N. Sims, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-005-F)

Historically, many connective tissues extracts have been shown to possess osteogenic capabilities. This study examines the ability of fresh, ground dentin to stimulate bone fill into periodontal osseus defects. Seven defects in four patients were exposed, debrided and filled with ground autogenous dentin obtained from non-savagable teeth. Following fill, soft tissues were replaced and held by sutures. Operated areas were clinically re-examined at one, three and six months.

An average of 60.1% decrease in periodontal pocket depth was achieved with only a 1.2 nm loss of gingival height by this experimental methods. Adjacent areas revealing lesser defects were treated by conservative methods. This treatment produced a 44% pocket reduction and a loss of 1.3 nm of gingival height. The experimental method proved superior in both pocket elimination and support of soft tisues to conventional controls. This study, however, should be considered as only a pilot study.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

2.0184, ACCELERATION OF WOUND HEALING

G.C. Battistone, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Basic Sciences, *Washington, District of Columbia* 20012 (DA0B6037)

Studies conducted by the Army in recent years show that 10-12 percent of combat wounds involve the maxillofacial apparatus. Further percent of noncombat injuries requireing hospital care involve the maxillofacial region. This results in the loss of approximately 1,000,000 man-hours per year. The research objective is to accelerate or otherwise improve healing of the combat maxillofacial wound, demonstrate cost effective measures by decreasing medical requirements and hospital stay and effect a rapid return of the soldier to duty.

Studies on the effects of biochemical and physical factors to include chelate complexes, cyclic amp, prostaglandins, scar inhibiting agents, in vivo growth factors and electric currents on the rate of healing in soft tissue and bone will be done. The mechanism of any beneficial alteration in healing effected will be investigated and pursued to human usage.

SUPPORTED BY
U.S. Dept. of Defense, Army,
Medical Research &
Development Command, Inst.
of Dental Research funds n.a.

2.0185, RECONSTRUCTIVE SURGERY FOR ORAL DEFECTS FOUND IN NAVAL PERSONNEL

J.T. Mellonig, U.S. Dept. of Defense, Navy, Naval Medical Research Inst., Clinical Sciences Div., *Bethesda, Maryland* 20014 (DN140033)

TECHNICAL OBJECTIVES: Most active duty Navy and Marine Corps personnel (greater than 90%) suffer from oral disease which results in destruction of bone and soft tissue in the oral cavity. These conditions represent a major military health problem, and may limit combat effectiveness and readiness. This investigation will search for and evaluate methods of reconstructing lost bone and skin with various bone and skin graft materials. The results will identify those graft materials and procedures that will have the highest degree of predictable success and potential for future application to military personnel.

APPROACH: The bone forming and wound healing potential of bone grafts, both freeze-dried and decalcified freeze-dried, will be assessed by implanting the graft materials into bony defects created in the oral cavities of non-human primates. Grafts will be evaluated microscopically, clinically and with X-rays over a 1-year period. Concomitantly, the potential of the grafts to elicit an immune response will be monitored using various immunological assays. Specific uses and the function of freeze-dried skin grafts in eliminating oral soft tissue defects will likewise be determined using similar methods of evaluation with the addition of autoradiography.

PROGRESS: Preliminary baseline data relative to the oral bony morphology and immunologic profile of non-human primates has been obtained. Bone defects have been created which are clinically comparable with the natural diseased state. A sufficient time interval has allowed these defects to stabilize as non-healing wounds. Reconstructive surgery with freeze-dried bone grafts is progressing as programmed.

SUPPORTED BY
U.S. Dept. of Defense, Navy,
Naval Medical Research &
Development Command,
National Naval Medical Center funds n.a.

2.0186, EVALUATION OF THERAPEUTIC AGENTS FOR THE PREVENTION OF ORAL BONE DESTRUCTION IN NAVY AND MARINE CORPS PERSONNEL

E.P. Leonard, U.S. Dept. of Defense, Navy, Naval Dental Research Inst., Histopathology Div., *Great Lakes, Illinois* 60088 (DN477027)

The purpose of this work is to provide safe and effective means for controlling oral bone destruction in Navy and Marine corps personnel. any therapeutic means which results in a reduction of bone loss, tooth mobility and pocket and abscess formation would by its Navy-wide application, correspondingly reduce patient man-hour loss for treatment, reduce the potential for diminished operational readiness under isolated conditions (e.g. Extended periods at sea or isolated areas) and virtually eliminate that disease as a cause of emergencies amongst operating Navy and Marine Corps forces. The technical questions being explored include (1) determining what specific agents offer significant promise in reducing oral tissue destruction, and (2) identifying the host mechanisms involved in its progression and/or exacerbation.

Tests will be conducted in a well defined animal model to test the potential benefits of several drugs which have the potential to reduce dental plaque formation, gingivitis, and their sequela, oral bone destruction. Groups of animals will be divided into either drug recipients or controls (placebo) and the progression (or lack thereof) of the destruction process will be measured by clinical, histometric x-ray and histopathologic analyses.

SUPPORTED BY
U.S. Dept. of Defense, Navy,
Naval Medical Research &
Development Command,
National Naval Medical Center funds n.a.

2.0187, WOUND HEALING OF THE SUPPORTING TISSUES OF THE TEETH OF NAVAL PERSONNEL

M.R. Wirthlin, U.S. Dept. of Defense, Navy, Naval Dental Research Inst., Clinical Investigation Dept., *Great Lakes, Illinois* 60088 (DN677136)

TECHNICAL OBJECTIVES: Naval dentistry performs over 400,000 surgical procedures a year involving the supporting tissues of the teeth. These treatment procedures done for oral disease and trauma have developed on a largely empirical basis, and as a result, remission, re-operation, and deformity are commonplace. The objective of this work is to develop a rational approach to surgical management of supporting tissues of the teeth which will limit deformity and improve oral health by assuring a reconstitution of the supporting tissues through healing by connective tissue new attachment.

APPROACH: This study will include histologic, roentgenographic, cell culture, and biochemical investigations of human periodontal tissues; and will document the healing response following injury, with particular emphasis on new attachment of connective tissue to root surfaces by cementogenesis. Standardized gingival wounds of simple incision and partial excision will be developed and healing studied in biopsies. Chemical and physical changes in the tooth root surface will be determined and tooth roots evaluated for viability of cell attachment in cultures on extracted teeth. Alveolar bone proper and cementogenesis at the gingiva-tooth root surface junction will be evaluated in biopsies by identification of mineral-exporting cell by special staining.

PROGRESS: Standardized gingival wounds have been evaluated histometrically and for rupture strength. Chemical analysis of these wounds has been completed. The accuracy of clinical measuring instruments was determined and a method of producing acrylic replicas has been perfected. A cell culture laboratory was established and procedural techniques are being perfected. One (1) technical report.

SUPPORTED BY
U.S. Dept. of Defense, Navy,
Naval Medical Research &
Development Command,
National Naval Medical Center funds n.a.

2.0188, QUANTITATION OF BONE ACTIVITY IN ALVEOLAR BONE OF RABBITS

N.N. Soni, Howard University, Graduate School, *2400 6th St. N.W., Washington, District of Columbia* 20001 (S06 RR 08016-090018)

This project is part of a broader program (RR 08016-09) whose summary states: A renewal application is made for continued minority Biomedical support for the Biomedical Interdisciplinary Project at Howard University. It consists of individual research elements with biomedical relevance and requests for support of strong undergraduate and graduate student research participation. The subject areas of Botany, Chemistry, Dentistry, Immunology, Psychology and Zoology are represented among 19 research project elements organized by individual faculty members or collaboratively among faculty in two or more disciplines.

Support is requested for visiting scientists to serve as a part of a Seminar-Science Conference component designed to promote University-wide communication among faculty and student scientists at Howard.

Overall, a program is proposed which will ultimately increase the biomedical research potential at Howard and add to the pool of minorities trained and prepared to perform at a high level in biomedical research.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health, Div. of
Research Resources funds n.a.

2.0189, THE BIOLOGY OF SKELETAL AND MINERALIZED TISSUES

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The broad, long range objectives of this Program Project are to acquire and communicate new, fundamental knowledge on the chemistry, molecular structure, organization and physiological function of the cells and extracellular matrix of connective tissues, with particular reference to bone, cartilage, dentin and enamel. Considerable effort will be directed to studies of tissue calcification and to the features which distinguish the skeletal and mineralized tissues from other connective tissues, since these specific characteristics are likely to play a critical role in defining their biological function. Our research projects cover all levels of anatomical hierarchy and molecular organization and the answers to important questions are being sought by integrating data from a wide diversity of scientific disciplines and techniques, including ultrastructural analysis, biochemistry, biophysics, and bioengineering.

We feel that such a multifaceted but concentrated research effort on the basic biology and pathology of the skeletal system at the molecular, cellular, tissue, organ and whole-organism levels will engender a more complete understanding of tissue calcification, calcified tissues and diarthrodial joints and provide a more rational basis for the diagnosis, treatment and prevention of the skeletal diseases that now disable a large part of our population.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Arthritis Metabolism & Digestive Diseases	$623,672

2.0190, RADIOIMMUNOASSAY OF PARATHYROID HORMONE IN THE RAT

R.H. Ophaug, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160068)

Pursuant to carrying out investigations on the effect of fluoride intake and magnesium deficiency of the level of circulating parathyroid hormone (PTH) in the rat, a radioimmunoassay system has been tested in our laboratory. Several antibodies against bovine-PTH have been evaluated and have been found to be unsuitable for measurement of PTH in rat serum although they yield good results for human PTH. An immunization program employing the immunization schedule described by Velitukaitis et al. (J. Clin. Endocrinology 33:988, 1971) is being initiated in an attempt to obtain a suitable antibody. Purified bovine PTH will be employed as the antigen.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$2,000

2.0191, THE EFFECT OF FLUORIDE ON ACUTE ZINC DEFICIENCY IN THE RAT

L. Singer, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160079)

For summary: see 1.0286.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$5,100

2.0192, VITAMIN A, FLUORIDE AND GLYCOSAMINOGLYCANS IN BONE

L. Singer, University of Minnesota, Minneapolis Campus, School of Medicine, Dept. of Biochemistry, *1305 Mayo, Minneapolis, Minnesota* 55455 (P01 DE 01850-160080)

Using 35S incorporation as an index of glycosaminoglycan synthesis in bone, the effect of fluoride intake and vitamin A deficiency on glycosaminoglycan metabolism has been studied in rats. Vitamin A deficiency results in a decrease in the rate of glycosaminoglycan synthesis in bone as evidenced by lower 35S/micrograms uronic acid ratios in the humeri epiphyses of vitamin A deficient animals compared to pair-fed controls. Elevated fluoride intake (10 ppm pr 50 ppm in the drinking water) had the opposite effect. Vitamin A deficient, pair-fed and ad libitum animals in the 0 ppm fluoride group had lower (p less than 0.01) 35S incorporation into bone than the corresponding animals receiving 10 ppm or 50 ppm.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$10,200

2.0193, THE MECHANISM AND TREATMENT OF PERIODONTAL DISEASE

P. Goldhaber, Harvard University, Boston Campus, School of Dentistry, Dept. of Periodontology, *188 Longwood Ave., Boston, Massachusetts* 02115 (P01 DE 02849-11)

Research will continue in five major areas: Project 1 - A. Factors influencing the enhancement or the inhibition of bone resorption and formation. B. Mechanism of action of various bone remodelinn factors. Project II - A. The role of collagenase and other factors influencing degradation of bone collagen. B. The effect of parathyroid extract and other bone resorption-stimulating factors on the nature of the new bone collagen formed in a bone remodeling system. Projeect III - A Pharmacological Approach to the Treatment of Periodontal Syndrome in Beagle Hounds.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

2.0194, STUDIES OF BONE CELL PROCESSES AND SYSTEMIC FACTORS IN ALVEOLAR BONE LOSS

D.J. Baylink, University of Washington, School of Medicine, Dept. of Medicine, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (P50 DE 02600-130028)

The proposed work deals with: 1) studies of three key bone processes: osteoclastic resorption, bone repletion, and the coupling between bone formation and resorption; and 2) a study in which the role of systemic factors in alveolar bone loss will be assessed from bone mass measurements of the distal radius in patients with periodontal disease, edentulous patients and normal subjects. Studies of osteoclastic resorption will be concerned with the interrelationships between 1,25-diOH-CC, PTH, and serum phosphorus on the process of bone resorption. With respect to bone repletion, we will investigate the possible roles of permissive hormones, mechanical stress, unidentified humoral factors, and osteogenic stem cells. Studies on coupling will seek to test the hypothesis that the coupling between formation and resorption is due to a counterregulatory mechanism modified by local factors and functioning to preserve bone mass. Because stem cells could figure importantly in all three of the above processes, a number of studies of osteogenic stem cells in vitro are proposed; including assessment of changes in stem cell proliferation and differentiation in response to local humoral agents implicated in alveolar bone loss.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $122,477

2.0195, EFFECTS AND FUNCTION OF THYROCALCITONIN AND VITAMIN D IN LACTATING AND SUCKLING RATS

S.U. Toverud, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Oral Diagnosis, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130088)

The effect of lactation on maintenance of calcium homeostasis is being studied by determining the roles of parathyroid hormone, thyrocalcitonin and vitamin D. The effects of parathyroid gland removal and thyroid gland removal and injections of parathyroid hormone and thyrocalcitonin on serum calcium and phosphate levels are being compared in lactating and non-lactating rats. Also under study are changes in the blood level of 1,25-dihydroxyvitamin D3 during lactation, changes in interfinal calcium absorptions, and the effects of maternal vitamin D deprivation on calcium metabolism and secretion of parathyroid hormone in the suckling rat pup.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $69,767

2.0196, TISSUE-MATERIAL INTERACTION IN IMPLANT MATERIALS

D.F. Taylor, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Operative Dentistry, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130179)

For summary: see 9.0077.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $11,967

2.0197, PHYSIOLOGICAL CONTROL OF THYROCALCITONIN SECRETION IN RATS

P.F. Hirsch, University of North Carolina, Chapel Hill Campus, Dental Research Center, Dept. of Pharmacology, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130192)

Experiments are designed to evaluate the role of endogenous calcitonin in: (1) Restricting bone loss in rats during periods of calcium deficiency and during lactation, and (2) in restoring bone mass after lactation and after refeeding calcium to rats previously fed a calcium-deficient diet. Mass of individual bones, as measured by dry weight, ash weight, and calcium content, as well as by total body calcium, will be compared in thyroidectomized and sham-operated rats with functional parathyroid transplants and with adequate thyroxine treatment. First, we will establish which strain of rats will best demonstrate the finding, reported by others, that the weight of the tibia after lactation is significantly less in calcitonin-deficient than in control rats. Then, the studies will be extended to include measurements of other bones and investigatons of possible mechanisms responsible for the effect; as, for example, effects of calcitonin on the gastrointestinal absorption of calcium, urinary calcium excretion and blood levels of calcium and phosphorous. In other experiments, the effect of calcitonin on the rate of restoration of bone mass lost during lactation will be examined in calcitonin-deficient rats (thyroidectomized at the end of lactation) and control rats.

The effect of calcitonin deficiency on the development of osteopenia in young growing rats on a low calcium diet will also be examined. In later experiments, the role of endogenous calcitonin on the restoration of bone mass in the osteopenic growing rats will be examined. In the latter studies, the sequence of events will be induction of osteopenia, thyroidectomy or sham-operation and feeding a diet with an adequate calcium content. These and other experiments will provide data necessary to establish functions for calcitonin and its effects under the stress of relative calcium deficiency during growth and lactation.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $52,177

2.0198, ENHANCEMENT OF BONE GROWTH BY PARATHYROID HORMONE (PTH)

M.A. Crenshaw, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Pedodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130194)

Since it appears that chronic low doses of parathyroid hormone (PTH) enhance the growth of long bones, we will determine if a similar effect of the hormone can be demonstrated on craniofacial bones. Such finding could be of great therapeutic value in repair of cleft palates and in other procedures requiring growth of new bone in the craniofacial area. Rats (6-weeks-old) will be injected daily with 5 units PTH. Blood calcium and phosphate levels will be monitored and at the end of weeks femurs, tibiae, mandibles and palatine bones will be assessed for mineral content and density and for incorporation of previously injected 3H-proline into collagen. Bone growth will also be evaluated using autoradiographic and histological techniques. Direct effects of PTH on bone growth will also be determined on cultured embryonic chick tibiae. Bones will be harvested from 7- to 10-day embryos and will be incubated for 2 to 7 days with or without PTH added to the medium (.001 - 1U/ml). After culture, these bones will be analyzed for changes in mineral and protein content and for changes in collagen synthesis. Some cultured bones will also be evaluated autoradiographically and histochemically.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $15,681

2.0199, VITAMIN D AND BONE

S.U. Toverud, University of North Carolina, Chapel Hill Campus, Dental Research Center, Dept. of Oral Diagnosis/Pharmacology, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130195)

The overall objective of this project is to determine if physiological amounts of vitamin D or any of its metabolites exert a direct action on bone cells during normal growth and maturation. Specific goals are: a. To evaluate the role of vitamin D in bone growth and bone mineralization. It is of particular interest to determine if the polar metabolites of vitamin D3, 25-hydroxycholecalciferol (25-OHD3), 1,25-dihydroxycholecalciferol (1,25-(OH)2D3), and 24,25-dihydroxycholecalciferol (24,25-(OH)2D3), can affect these processes by a direct action on bone. b. To determine if physiological amounts of vitamin D or its metabolites can participate in the hour-to-hour regulation of serum Ca by a direct action on bone.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $46,512

2.0200, STUDIES OF NUTRITIONAL INDUCTION AND PREVENTION OF OSTEOPOROSIS

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II. PERIODONTAL DISEASE

The cause(s) and pathogenesis of osteoporosis are subject to debate, although this bone disease is common and of worldwide medical and dental importance. Since matrix and mineral are reduced proportionally in this disorder, it seems clear that nutritional factors must play a role in its development. Furthermore, with the exception of osteogenesis imperfecta, osteoporosis is not hereditary, and hope for prevention and treatment lies in elucidating the role of nutrients and other factors in adult bone metabolism.

There are few available animal models of osteoporosis. The guinea pig requires dietary vitamin C and because of this requirement has been utilized for connective tissue studies such as wound healing and bone growth. Since we have developed an adequate purified diet which is readily accepted by the guinea pig, it should be possible to induce osteoporosis by specific alterations in the diet and to study interrelationships between nutrients with respect to development and prevention of this disorder.

We will perform a series of multifactorial experiments utilizing the methods of experimental nutrition, light and electron microscopy, radiography and chemical analysis to bring new understanding to the problems of bone formation and loss. Use of analysis of variance of data obtained in factorial experiments will enable us to discern the importance of interaction between specific nutrients in development and treatment of osteoporosis.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $20,408

2.0201, RELATION OF INFLAMMATION MEDIATORS TO DESTRUCTIVE PERIODONTAL DISEASES

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Mechanisms of destruction of the supporting structures of the teeth have been postulated in numerous papers. Little direct evidence to support or refute these hypotheses has been provided. In the present investigation, suspected mediators of bone loss and periodontal disease will be measured in sites of defined active disease status. These mediators include: prostaglandins, osteoclast activating factor (OAF), endotoxin, and bone stimulation resorption factor (BSRF). The presence of these substances will be related to clinical and microbiologic parameters in order to establish their possible relationship to the periodontal disease process and suggest alternative modes of parmacologic therapy directed toward antagonism of their action.

Tissues taken from the advancing disease sites will be collected at the time of periodontal surgery for assay of their mediator content. Measurement of Prostaglandin E levels will be by radioimmunoassay and compared with the response elicited in bone resorption assay. The validity of current hypotheses related to the destructive mechanism will be tested by evaluation of the relative content of local mediators of tissue destruction and comparison with the clinical and microbiologic observations.

The pharmacokinetics of antimicrobial compounds administered in the therapy of destructive periodontal disease will be examined. The current usage of such agents is based largely on anecdotal information. The current usage of such frequency, and duration of therapy will be optimized by determination of local concentrations within the periodontal pockets.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $138,958

2.0202, HORMONES, BONE CELL INTERACTIONS AND BONE MINERALIZATION

H. Schraer, Pennsylvania State University, University Park Campus, School of Science, Dept. of Biochemistry & Biophysics, *211 Whitmore Lab., University Park, Pennsylvania* 16802 (R01 DE 01764-17)

Bone cell differentiation and bone synthesis induced by estrogen administration to male Japanese quail will be used to study several facets of these processes. Among these studies will be the analysis of bone samples taken when 3H-glucosamine and 35SO4 uptake increase sharply. This may allow us to discern the spectrum of glycosaminoglycans and other labeled compounds in order of their appearance during bone matrix formation. In another study the femurs of birds will be removed after specific periods of estrogen treatment and incubated with different isotopically labeled compounds to determine whether or not differentiation and bone synthesis will continue under in vitro condition. In further studies, samples of embryonic chick femur taken during early phases of mineralization will be used to study the intra and extracellular distribution of several elements important in the mineralization process. Comparison of this system with other calcification systems such as the avian shell gland will be made. Electron microprobe analysis of frozen thin sections and inert dehydration and embedding procedures will be used in these investigations.

BIBLIOGRAPHIC REFERENCES: Clermont, C.P. and Schraer, H.: Effect of Estrogen on the Rate on 59Fe Uptake by Hemopoietic Tissue in Japanese Quail. Am. J. Physiol. In Press, 1979. Gay, C.V., Schraer, H. and Hargest, T.E.: Ultrastructure of Matrix Vesicles and Mineral in Unfixed Embryonic Bone. Metabolic Bone Disease and Related Research 1:1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$86,357

2.0203, INDUCTIVE SUBSTRATES OF TOOTH AND BONE

M.R. Urist, University of California, Los Angeles Campus, School of Medicine, Dept. of Surgery, *2025 Zonal Ave., Los Angeles, California* 90024 (R01 DE 02103-15)

The proposed research into the physiology of osteoinduction has clinical and experimental objectives. The clinical objective is to prepare osteoinductive dentin and bone alloimplants for patients with jaw bone and long bone defects caused by tumors, infections, injuries, and congenital malformations. The experimental objective is to isolate and characterize the bone morphogenetic protein (BMP) in dentin and bone matrix responsible for osteoinduction. BMP is bioassayed by implantation of lyophilized samples in a muscle pouch in gelatin capsules and double-walled diffusion chambers of pore size as small as 0.025 microns in allogeneic rabbits, rats and mice. While there are many systems for cell-cell interactions between mesenchymal cells and uroepithelium or HeLa cells or amnion or transformed fibroblasts, only one system produces bone from interaction of mesenchymal cells with a chemically defined substratum. This system consists of interaction of mesenchymal cells or young fibroblasts with either dentin or bone or osteosarcoma matrix. In tissue culture, the product is cartilage while in vivo, bone and bone marrow. Knowledge of the physiology of the inductive matrix is applied in the preparation of a chemosterilized, autolysed antigen-extracted, allogeneic (AAA) bone graft. The experimental program is to characterize the biochemical components of dentin, bone and osteosarcomas responsible for the osteoinductive response in adult rabbits, rats, and mice. The experiments are designed to separate insoluble bone morphogenetic protein (BMP) from bone matrix by melting bone collagen at 25 degress C in LiCl and to isolate soluble BMP at 37 degress C by hollow fiber ultrafiltration. Soluble BMP is characterized by chemical analyses, gel filtration, gel electrophoresis, immunophoresis, column chromatography, amino acid analyses, and amino acid sequenation. A solubilized BMP is also obtained from cortical bone matrix powder by incubation at 37 degress C in buffered solutions containing endogenous sulfhydryl enzyme inhibitors and a bone matrix glycoprotein carrier. Bone matrix BMP will be compared with a soluble BMP in the media of osteosarcoma cell cultures.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$167,181

2.0204, INTERACTION OF FLUORIDE WITH MINERALS IN MAN

H. Spencer, Loyola University of Chicago, Maywood Campus, Loyola University Stritch School of Medicine, Dept. of Medicine, *2160 S. 1st Ave., Maywood, Illinois* 60153 (R01 DE 02486-11)

The studies will be carried out in patients with chronic renal disease in order to investigate the metabolism of fluoride in patients in whom the function of the major organ of fluoride excretion, the kidney, is impaired. The dietary fluoride intake and the renal and intestinal excretions of fluoride will be determined for several weeks under strictly controlled dietary conditions in the Metabolic Research Ward in order to assess the retention of fluoride under dietary conditions which are appropriate for these patients. The fluoride intake will be due to the fluoride content of the diet and the intake of fluoridated drinking water. These studies will be carried out during normal calcium intake and during the addition of calcium to the constant diet. Attempts will be made to study the changes in fluoride metabolism during different phases of renal impairment in the same subject in order to correlate the changes in fluoride metabolism with the extent of renal impairment. The effect of medications which are commonly used for the treatment of these patients will be investigated on the metabolism of fluoride of these patients. Examples of these drugs are diuretics and antihypertensive compounds, used alone or in conjunction with the antacid aluminum hydroxide which is commonly used to decrease the elevated serum phosphorus level in patients with chronic renal disease.

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SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
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2.0205, THE ORIGIN AND ROLE OF OSTEOCLASTS IN TOOTH ERUPTION

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The major goals of this investigation include the determination of the effects of a neonatal cure of osteopetrosis on tooth eruption and the determination of the fate of radioactively labeled donor cells during the recovery from osteopetrosis.

Neonatal cure of osteopetrosis will be accomplished in newborn rats whose genotype has been determined radiographically after hypothermic anesthesia. Spleen cells from normal donors will be injected into ia littermates after whole-body radiation and the effects on eruption of incisors and first molars noted by inspection and histologically. If the teeth do not erupt, we shall attempt to accelerate osteoclastic differentiation and bone resorption by injection of parathyroid extract and vitamin D in doses that promote bone resorption. The same sequence will be repeated in animals that are not irradiated, to determine if radiation is required for the neonatal cure as it is for older rats. If the transplanted cells are not rejected in the newborn and result in a cure, this procedure will be useful in future studies on the origin of osteoclasts.

The possibility that cells from normal rats cure the disease by transforming into competent osteoclasts will be investigated. We shall labor donor cells in vivo by injection of 3H-thymidine at 8-hour intervals for 3 or 4 days. This should label all dividing cells in the thymus or spleen, from which the mononuclear cells will be isolated by density gradient centrifugation. The fate of these labeled cells will be followed autoradiographically in a mutant host whose osteoclasts are developing ruffled borders and resorbing bone. Appropriate timing of the interval after cell injection should permit observation of labeled nuclei in ia osteoclasts if the cure is mediated by direct transformation of donor cells into osteoclasts.

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Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
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2.0206, CELLULAR AND DEVELOPMENTAL CONTROL OF CALCIFICATION

A.I. Caplan, Case Western Reserve University, Case Inst. of Technology, Dept. of Biology, *2040 Adelbert Rd., Cleveland, Ohio* 44106 (R01 DE 04008-05)

The objective of the proposed experimentation is to obtain information on the cellular and molecular aspects of bone development and biological calcification in the embryonic chick limb. A combined morphological (light and electron microscopic) and biochemical approach is being used in analyzing both in vivo development and a limb cell tissue culture system. This tissue culture system is initiated by plating undifferentiated chick limb mesenchymal cells into culture. We have followed the emergence of specific foci of calcium phosphate deposition, the parathyroid hormone stimulation of adenylate cyclase, cAMP levels, alkaline phosphate activity, collagen biosynthesis, and proteoglycan biosynthesis. We propose to continue and expand these studies in order to attempt to provide experimental details of the emergence of the osteogenic phenotypes, to ascertain what factors influence this emergence and to thus provide an understanding of the chemical, cellular and developmental mechanisms which govern the process of bone formation.

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National Inst. of Health,
National Inst. of Dental
Research $84,567

2.0207, DIETARY PROTEIN, OSTEOPOROSIS AND PERIODONTAL DISEASE

L.H. Allen, University of Connecticut, Storrs Campus, School of Agriculture & Natural Resources, Dept. of Nutritional Sciences, *Storrs, Connecticut* 06268 (R01 DE 04295-03)

It is well established that dietary protein causes calciuria. We have shown that a high protein diet induces hypercalciuria, and thereby a negative calcium balance, in both humans and laboratory animals. The negative calcium balance occurs even in the presence of adequate calcium intakes, and has potential significance for the development of osteoporosis and periodontal disease in occidental populations which consume large amounts of dietary protein. We propose to use animal models to determine the short-term effect of high protein diets on calcium metabolism and bone calcium turnover, and their long-term effect on bone calcification and periodontal disease. Our preliminary research indicates that dietary protein impairs the fractional reabsorption of calcium by the kidney. We propose to investigate the mechanism by which this occurs in both human subjects and animal models.

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Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

2.0208, CELLULAR AND MOLECULAR ASPECTS OF MINERALIZATION

H. Schraer, Pennsylvania State University, University Park Campus, School of Science, Dept. of Biochemistry & Biophysics, *211 Whitmore Lab., University Park, Pennsylvania* 16802 (R01 DE 04345-04)

The objectives of the proposed research are to determine the intracellular location of several constituents and the route of translocation of calcium, phosphorus and other elements in bone cells during bone formation and resorption. The methodology for these studies is critical and consists of electron microprobe analysis of bone prepared by ultracryomicrotomy. Autoradiography and immunohistochemical procedures will be used for detecting carbonic anhydrase at the electron microscope level in osteoclasts and other tissues. The influence of parathyroid hormone and calcitonin on carbonic anhydrase levels in osteoclasts will be assessed.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $83,096

2.0209, DENTAL DISEASE AND OSTEOCLASTIC BONE RESORPTION

A.J. Kahn, Washington University, School of Dental Medicine, Dept. of Biomedical Sciences, *4559 Scott Ave., St. Louis, Missouri* 63130 (R01 DE 04629-03)

Grafts of Japanese quail limb and bone rudiments onto the choriallantoic membranes (CAM) of chick embryos are being used to study the linkage of skeletal cells. Such tracing is possible because the morphology of the quail interphase nucleus is distinctly different from that of the chick.

Skeletal cell lineage has been evaluated in (1) bone rudiments transplanted before and after the establishment of the marrow cavity, (2) bone rudiments fractured several days after transplantation, and (3) grafted pieces of perichondrium-free epiphyseal cartilage. These experiments have shown that while osteoblasts are derived from precursors located within the bone rudiment, osteoclasts have their origin from the blood vascular system. In addition, these studies have demonstrated that fractured embryonic bones heal rapidly and without callus formation, and that chondrocytes may survive hypertrophy and redifferentiate into osteoblasts.

Experiments have recently been initiated in which the quail-chick chimeric system will be used to establish the first appearance of the osteoclast during embryonic development, and to determine the life span of the osteoclast. The marker system will also be incorporated into experiments designed to identify and isolate the hematopoietic precursor of the osteoclast.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$110,999

2.0210, CELLULAR EVENTS IN BONE REMODELING OF TOOTH MIGRATION

H. Rasmussen, Yale University, School of Medicine, Dept. of Internal Medicine, *333 Cedar St., New Haven, Connecticut* 06510 (R01 DE 04724-03)

This work is aimed at determining the cullular events in bone remodeling and the fate of nuclei in the osteoclasts, using alveolar bone and tooth migration as a model. Similar in vitro studies are also conducted with either tissue cultures or isolated bone cells. The techniques used are mainly dynamic bone histomorphometry on undecalcified thin sections with double fluorescent labels, electron microscopy and autoradiography. The time course of early effects of parathyroid hormone and calcitonin on the osteoclast population and the number of nuclei they contain have been studied during the first year of this project. During the current year, the effects of three diphosphonates Azacycloheptane-2,2-Diphosphonic acid (AHP), Dichloromethylene Diphosphonic acid (Cl2MDP) and 3-Amino-1-Hydroxy-Propane-1,1-Diphosphonic acid (APD) at concentrations ranging from 0.05 to 50.0 mg/Kg during 5 to 10 days of treatment have been studied. All three diphosphonates induced various degrees of inactivation of the osteoclasts associated with an increase in their number and an increase in the number of nuclei they contain. The total number of nuclei in the osteoclastic pool was therefore increased 3-fold. The effects of PTH on this accumulation of nuclei and then the effects of calcitonin will be studied next year in order to follow the fate of osteoclast nuclei. Of interest is the fact that tooth migration was maintained with a normal amount of bone matrix being formed despite a decrease in the calcification rate and in the resorption rate. In vitro studies on fetal rat long bones conducted this year indicated the need for having more homogeneous bone cell populations in order to separate the reactions of osteoclasts and osteoblasts to different agents. Studies using rabbit long bone fragments are planned in the coming year.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$96,099

2.0211, LOCALIZATION IN GINGIVA OF BONE RESORPTION MEDIATORS

K. Nuki, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Periodontics, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 04728-02)

Loss of alveolar bone is associated with chronic gingival inflammation and periodontal disease. Previous studies have shown that both healthy and inflamed gingival samples can produce bone-resorbing factors when cultured. The major objective of this study is to gain insight into some aspects of the mechanism of bone loss in periodontal disease, by determining as closely as possible which structural components of inflamed gingiva are associated with in vitro bone resorbing activity.

The gingival tissues to be examined will come from beagle dogs in various stages of controlled inflammation, both with and without radiographic evidence of alveolar bone loss. Bone resorbing activity will be measured in freeze dried, microdissected, weighed samples, by means of 45Ca release from labelled fetal rat bones in culture. The results, expressed as the ratio of 45Ca released in each cultured and that remaining in the test bone, will be compared with non-inflamed control tissue and statistically analyzed for validity or otherwise.

Although the main part of the study will be carried out on tissue from dogs, in the final phase of the study the bone resorbing activity of human gingiva will be compared with that found in the animal model. A comparison will be made of bone resorbing activity in both adult and childhood gingivitis.

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2.0212, RELATION OF INFLAMMATION TO BONE RESORPTION

C.L. Trummel, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Periodontics, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 04885-03)

Oral microorganisms colonizing the tooth surface and gingival sulcus are acknowledged to be the primary cause of periodontitis. This research project is aimed at identifying and characterizing the chemical mediators and cellular mechanisms responsible for the loss of tooth-supporting tissue so characteristic of this disease. Studies are in progress or will be initiated to approach the following specific aims: 1. identification of bacterial products which can directly stimulate bone resorption. Bacteria associated with periodontal disease are being tested for products which can stimulate resorption of cultured bone rudiments. A soluble material from Actinomyces viscosus has been found which is a potent stimulator in this model system; its chemical nature is now being investigated. Lipopolysaccharide preparations from various Gram-negative organisms isolated from deep periodontal pockets will be tested and compared for bone resorptive potential. 2. identification of factors which can stimulate macrophage secretion of collagenase. Macrophages are consistently found in the chronic inflammatory lesion of periodontitis. A material prepared from Actinomyces viscosus has been found which stimulates cultured macrophages to secrete collagenase. This factor and its action on macrophages will be further evaluated. Products from other bacteria will be similarly examined using this model. 3. identification of the cellular source of osteoclast activating factor (OAF). OAF is a material produed by activated peripheral blood mononuclear cells which can stimulate bone resorption in vitro. Using enriched populations of cultured lymphocytes and macrophages, experiments will be conducted to determine which of these cells produces OAF and the nature of the cellular interactions which occur.

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2.0213, MECHANISMS OF BONE RESORPTION IN CHRONIC PERIODONTITIS

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The pathogenesis of chronic periodontitis involves the conversion of an established gingival lesion to an advanced periodontal lesion which most often is associated with extensive bone loss. Recently, both receptor and effector components of the host immune system have been implicated as causal factors in the process of bone resorption seen in various pathologic entities such as chronic periodontitis. The series of experiments proposed herein will explore the interaction and potential regulatory involvement of elements of the immune response with the process of bone resorption. We shall examine the role of cellular elements of the immune system (i.e. lymphocytes and mononuclear phagocytes) and immune effector molecules (e.g.,lymphokines such as the osteoclast activating factor OAF) in bone resorption, as well as explore aspects of immune function and bone cell function in animal mutants (osteopetrotic mice) which lack normal bone resorption. We propose to conduct the following types of experiments: (1) transplantation of enriched populations of hematopoietic tissue cells between normal and osteopetrotic mice to study the origin of the cellular defect in bone resorption; (2) in vitro studies of immune function in lymphocytes and mononuclear phagocytes in osteopetrotic mice; (3) hormonal regulation of various functional parameters in mononuclear phagocytes related to bone resorption; (4) studies of lymphokine production in normal and osteopetrotic mice and its role in bone resorption; (5) mononuclear phagocyte chemotaxis and its relationship to bone resorption; (6) comparative studies of functional parameters in isolated bone cell populations of normal and osteopetrotic mice obtained by sequential enzymatic dissociation.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$118,183

2.0214, METABOLIC PATHWAYS IN BONE

D.V. Cohn, University of Kansas, Medical Center, School of Medicine, Dept. of Biochemistry, *39th St. & Rainbow Blvd., Kansas City, Kansas* 66103 (R01 DE 05209-02)

We propose to study in culture two biochemically and morphologically distinct populations of bone cells, CT cells and PT cells that respond in distinctly different manners to parathormone and calcitonin. The parameters measured (and the cell type in which parathormone produced a change) were: acid phosphatase, hyaluronate synthesis, mineral and matrix resorption from dead bone (CT cells); alkaline phosphatase, citrate decarboxylation, prolyl hydroxylase, collagen synthesis and hydroxylation (PT cells); cAMP (CT and PT cells). On the basis of the basal activities and hormone-induced changes, we provisionally identified the CT cells as osteoclasts and/or osteocytes and the PT cells as osteoblasts. We propose to further characterize these bone cells by determining their growth and development in culture, the sites where they existed in situ prior to removal from the calvaria and the degree of heterogeneity of the isolated populations. We also plan to study the biochemical changes induced by parathormone and other bone-active hormones in order to better realize the biochemical bases for these alterations. Finally, we will measure the binding and interaction of parathormone and other agents with the isolated bone cells and bone-cell membranes.

BIBLIOGRAPHIC REFERENCES: Cohn, D.V. and Wong, G.L. (1978) The Actions of Parathormone, Galcitonin and 1, 25-Dihydroxycholecalciferol on Isolated Osteoclast-and Osteoblast-Like Cells in Culture. In Endocrinology of Calcium Metabolism (D.H. Copp and R.V. Talmage, eds.) Excerpta Medica, Amsterdam, pp. 241-255. Cohn, D.V. and Wong, G.L. (1978) The Effect of Parathormone on Collagen Formation in Isolated Bone Cells, Third International Workshop on Clacified Tissues, Kiriat Anavim, Israel, March 5-9, p. 28 (abstract)

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2.0215, REGULATION OF COLLAGENASE AND BONE RESORPTION

S. Sakamoto, Harvard University, Boston Campus, School of Dentistry, Dept. of Periodontology, *188 Longwood Ave., Boston, Massachusetts* 02115 (R01 DE 05255-01)

This new proposal consists of biochemical and histological approaches to the mechanism of regulation of tissue collagenase. Our main aim is to gain new knowledge of tissue collagenase of bone and periodontal tissues in health and disease and the results will be of basic value in developing a method to control and prevent bone resorption, thereby preventing alveolar bone loss in periodontal disease. The objectives are: 1. To study the latency of bone collagenase and the mechanism of its activation by isolating the enzyme, its latent form, inhibitor and activator. 2. To study the levels of tissue collagenase, in its active and/or latent forms of various cells and subcellular fractions derived from bone and periodontal tissues. Radioimmunoassay using specific antibody produced against mouse bone collagenase is our method of choice. 3. To study the possible capacity of anti-collagenase and other collagenase inhibitors to inhibit bone resorption in tissue culture in order to examine the role of this enzyme in the mechanism of bone resorption. 4. To study the rate of synthesis of collagen and collagenase in established fibroblast cell line, 3T6, and in isolated bone and gingival cells. The collagen synthesis is assayed as bacterial collagenase-digestible radioactive protein or by measuring labeled hydroxyproline after isolation by amino acid analysis and the amount of enzyme by radioimmunoassay.

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2.0216, THE ROLE OF LYMPHOID CELLS IN ALVEOLAR BONE RESORPTION

G.B. Schneider, University of Massachusetts, Medical School at Worcester, School of Medicine, Dept. of Anatomy, *419 Belmont St., Worcester, Massachusetts* 01604 (R01 DE 05291-01)

Bone resorption is accomplished by two cellular elements of the skeletal system; osteoclytic osteocytes, the primary mediators of the skeletal contribution to mineral homeostasis, and osteoclasts, surface cells primarily concerned with bone remodeling for mechanical strength. The ia (incisors absent) rat is a mutant that has a disease known as congenital osteopetrosis--a skeletal defect resulting from an abnormal accumulation of bone due to decreased bone resorption. This mutant has osteoclasts, but they are abnormal, lacking a ruffled border--the site of normal bone resorption. Evidence from our laboratory indicates that normal osteoclastic function and bone remodeling can be restored in the ia mutant by transplanting mononuclear cells isolated from the spleen and thymus of normal littermates. I propose to determine whether the transplanted cells are the precursor of the osteoclast by transplanting mononuclear cells from normal littermates, labelled with 3H-thymidine, into ia mutants, to see if labelled osteoclastic nuclei can be identified in alveolar bone. An alternative hypothesis is that the cells may be providing a local influence or cellular product that modulates normal osteoclastic activity. The possibility can be tested by transplanting lethally-irradiated, mitotically-inhibited, or differentiation-inhibited mononuclear cells from normal littermates into ia rats. The mononuclear cellular population will be further subdivided into monocytes and various subpopulation of lymphocytes to further deliniate the cellular source of the cure. Finally, the scope of the disease will be investigated by evaluating the other phagocytic cells in the ia rat to determine if the cellular defect is found only in the osteoclast or present in some hematopoietic stem cell, resulting in a more generalized defect.

These experiments should be useful in understanding normal and modulating abnormal osteoclastic function, and could be relevant to the treatment of a number of bone pathologies such as osteoporosis (loss of bone) and periodontal disease--the irreversible loss of alveolar bone. The most direct application of this study is the possibility of using the transplantation of mononuclear cells to cure the malignant-juvenile form of human osteopetrosis.

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2.0217, STUDIES INTO THE METABOLISM OF PARATHYROID HORMONE

P.J. Sammon, University of Kentucky, School of Dentistry, Dept. of Oral Biology, *Limestone & Euclid, Lexington, Kentucky* 40506 (R23 DE 04280-03)

Parathyroid hormone (PTH) has been implicated as a systemic factor that increases alveolar bone resorption in periodontal disease. Recent radioimmunoassay evidence indicates that there are multiple metabolites of PTH in the circulation, some of which may possess biological activity related to this disease, thus indicating that a more detailed investigation into PTH peripheral metabolism is needed.

Our development of a simple electrolytic iodination procedure for the production of 125I-tyrosine-labeled PTH possessing apparently full biological activity has prompted us to start on an investigation of the metabolism of PTH. A series of preliminary experiments indicated that 125I-PTH administered to rats was deposited very rapidly in three organ systems only: bone, kidney and liver. As indicated by increasing solubility in trichloracetic acid, the hormone seemed to be rapidly metabolized at the sites of deposition. Based on this information, quantitative extraction and gel filtration procedures were developed for the characterization of metabolites. It was found that intact hormone predominated in the circulation but was cleared very rapidly. There was also evidence of fragmentation to polypeptides of molecular weights of 6,000, 4,500 and 2,500. Whether these fragments are biologically active or represent catabolism of the hormone will be the subject of these investigations.

We have recently modified the iodination procedure to label the histidine residues of the hormone molecule. Further studies with this more uniformly labeled tyrosine-histidine hormone will facilitate the detection of the smaller amino terminal fragments in the circulation and organs of distribution in a way previously not possible.

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2.0218, HISTOCHEMISTRY OF CADMIUM AND ZINC IODIDE OSMIUM

S.W. Whitson, Southern Illinois University, Edwardsville Campus, School of Dental Medicine, Dept. of Biomedical Sciences, *Edwardsville, Illinois* 62025 (R23 DE 04509-03)

Cadmium iodide osmium (CdIOs) staining for acidic phospholipids on cartilage membranes, improved by cysteine soak and hexylene glycol embedding intermediate, will be further investigated with phospholipase, phospholipase inhibitors and quantitation. In the gut, specific phospholipids (fed to rats) will be coupled with this improved method to test for any phospholipid staining specificity.

To confirm that zinc iodide osmium (ZnIOs) stains for R-SH or R-S-S-R groups, research will investigate effects of -SH inhibitors and electron transport chain inhibitors on staining the inner matrix of isolated mitochondria.

The nature of copper iodide osmium (CuIOs) stained intramitochondrial precipitates seen only in mononuclear preosteoclasts and newly formed osteoclasts will be studied with key hormones and suspected inhibitors.

Comparing ferrous iodide osmium (FeIOs) used with FeCl3 plus K3Fe(CN)6 to colloidal iron and ferric hydroxychloride will evaluate our simplified, improved technique for staining the glycoprotein halyx.

Selenium iodide osmium (SeIOs) will be investigated to ascertain its peroxidase or lipase specificity.

Substitution of fluoride for iodide in Zn and Cd complexes will determine whether varying halides affects stain specificity.

Cation-halide osmium complexes will be tested in animal model systems of bone repair, hormonal control of adult bone metabolism and nutritional deficiency.

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Research $0

2.0219, PROSTAGLANDINS AND THROMBOXANE IN PERIODONTAL DISEASES

P.Y. Wong, University of Tennessee, Center for the Health Sciences, School of Basic Medical Sciences, Dept. of Pharmacol, *800 Madison Ave., Memphis, Tennessee* 38163 (R23 DE 04591-01A1)

The biochemical aspect of the research proposal is to investigate the biosynthesis and metabolism of prostaglandins and thromboxane in gingival tissues. Preliminary studies had shown that prostaglandin E2 levels are elevated in diseased human gingiva and may therefore participate in the pathogenesis of periodontal disease.

Subcellular fractions of the gingival tissue obtained from patients with periodontal disease will be used for assays of the enzyme (phospholipase, PG synthetase and cyclo-oxygenase and thromboxane synthetase) which are intimately involved in the biosynthesis of prostaglandins and thromboxane. The endoperoxide intermediates PGG2 and PGH2 will be isolated and their biological activity evaluated. The mechanism for the formation of thromboxane A2 and hydroxy fatty acid will also be examined. In the study of prostaglandin metabolism, 14C or 3H labeled PG will be used as substrate, and the activities of the metabolic enzymes (15 OH-dehydrogenase, delta 13,14 reductase and PGE 9-ketoreductase) will be measured. The sensitivity of the PGE 15 OH-dehydrogenase and PGE 9-ketoreductase to different vasoactive peptides and steroid hormones will be given special attention.

Further investigations of the release and ultimate fate of these vasoactive lipids will then be related to the possible physiological mechanism for the regulation of the inflammatory process and bone resorption in periodontal disease.

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Research $0

2.0220, PARATHYROID AND VITAMIN D CONTROL OF BONE AND KIDNEY

D.L. Carnes, University of Missouri, Columbia Campus, School of Medicine, Dept. of Pharmacology, *M228 Medical Sciences, Columbia, Missouri* 65201 (R23 DE 04601-03)

The research is designed to test, on the cellular level, a proposed mechanism for the impaired target tissue response to parathyroid hormone in the D-deficient animal. The hypothesis is (1) the hypocalcemia which occurs as a result of D-deficiency induces secondary hyperparathyroidism and (2) the resulting chronic high level of circulating parathyroid hormone subsequently alters the parathyroid hormone-sensitive adenylate cyclase system of target cells. Two cell types will be studied: (1) the isolated renal cortical tubule from rat kidney and (2) the isolated bone cell from newborn rat calvaria. Companion studies will be performed in vitro with tissue preparations from the same sources. The objectives of the research are: (1) to compare the responses of adenylate cyclase from both bone and kidney during D-deficiency (2) to ascertain whether or not the impaired parathyroid hormone-dependent adenylate cyclase activity during D-deficiency (2) to ascertain whether or not the impaired parathyroid hormone-dependent adenylate cyclase activity during D-deficiency is reflected in altered cellular c-AMP levels and parathyroid hormone responsive cell functions (3) to mimic the proposed action of parathyroid hormone in vitro by exposing the cells to chronic high levels of the hormone and (5) to directly study membrane receptors in these cells by assessing the binding of 125I-parathyroid hormone to membranes prepared from these cells.

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2.0221, BONE CELL CALCIUM REGULATION

R.M. Dziak, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (R23 DE 04637-03)

We propose to extend our studies on the role of intracellular calcium in the regulation of bone resorption using an isolated rat bone cell system. We will study the effects of calcitonin, a well characterized inhibitor of bone resorption, on calcium transport. Our preliminary studies on bone cell membrane purifications will also be continued. The purified membrane preparations will be used to investigate the role of Ca-ATPase in calcium efflux from bone cells.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0222, ROLE OF GAMMA-CARBOXYGLUTAMIC ACID IN BONE AND ENAMEL

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Gamma-carboxyglutamic acid (Gla) is synthesized post-translationally in a vitamin K-dependent and CO2-requiring enzymatic reaction in the microsomal fraction of liver, kidney and bone tissue cells. Gla is a specialized calcium-binding amino acid which mediates calcium and phospholipid dependent protelytic conversion in prothrombin to thrombin. Gla residues are found in a unique protein in bone named osteocalcin which has been characterized as a 6500 MW peptide containing 2 Gla residues/molecule. The function of osteocalcin in bone is unknown. This study proposes to determine its possible role in mineralization functioning either as a proenzyme, an inhibitor or a nucleating agent or a calcium transport protein. The microsomal osteocalcin substrate will be isolated and characterized to determine if osteocalcin-precursor is synthesized and undergoes vitamin K dependent carboxylation as the 6000 dalton peptide or as a higher molecular weight protein. To study the effect of vitamin K deficiency on bone mineralization processes, density-fractionation of ground bone will be performed to separate the least mineralized components from high density bone. A comparison of the distribution of fractions from densities of 1.4-2.1 g/cc in normal and vitamin K deficient bones will reveal if mineralization has been antagonized, either increased or decreased. In addition to these studies, clinical studies measuring urinary Gla excretion levels in patients with various metabolic disorders are being pursued. Both free and peptide bound Gla will be quantitated in 24 hour urines of patients with osteoporosis, Paget's disease of bone, osteomalacia and ectopic calcification disorders. The observed changes in urine Gla with a certain disorder may lend some insight into the functional nature of osteocalcin. Gla-protein(s) are also found associated with ectopic calcifications such as atherosclerotic plaque and scleroderma and may be responsible for the deposition of calcium. Their isolation and characterization is in progress.

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SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$30,909

2.0223, ALVEOLAR BONE IN EXPERIMENTAL RENAL INSUFFICIENCY

S.K. ElMofty, Washington University, School of Dental Medicine, Dept. of Pathology, *4559 Scott Ave., St. Louis, Missouri* 63130 (R23 DE 04755-03)

The widely spreading use of maintenance hemodialysis and the prolongation of life of uremic patients has been accompanied by an increase in incidence of renal osteodystrophy. Recently attention has been focused on the attending periodontal problems of these patients. This study is designed to investigate the effects of experimentally induced renal insufficiency on the alveolar bone and the periodontium of adult female beagle dogs. Changes in the alveolar bone are compared to those occurring in other parts of the skeleton. The effects of uremia on bone are quantitated radiographically and by histomorphometric techniques. Time spaced tetracycline labeling is used for the study of the kinetics of bone turnover. The periodontium is clinically evaluated and periodontal index scores (PI) and gingival sulcus depth are determined.

The efficacy of vitamin D as a therapeutic agent is investigated.

BIBLIOGRAPHIC REFERENCES: Small, C., Hruska, K.A., Teitelbaum, S.L. and El-Mofty, S.K.: The Alveolar Bone and the Periodontium in Experimental Renal Insufficiency. J. Dental Res., in press, 1979.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $29,877

2.0224, THE ROLE OF MACROPHAGES IN IN VITRO BONE RESORPTION

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In experiments using tissue culture methods to grow (newborn) mice calvaria in association with ellicited peritoneal macrophages (isolated from adult mice) a 23 percent decrease of calcium in the calvaria was observed. This response was measured after 7 days in culture. Scanning and transmission electron microscopy revealed many macrophages attached to the surface of the bone matrix. They were closely associated with the matrix surface but did not resemble osteoclasts, except for occasional multinucleated cells. It is concluded that macrophages resorb bone in this system but that it is different from osteoclastic bone resorption.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
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Research $30,387

2.0225, OSTEOCLAST SPECIALIZATIONS IN BONE RESORPTION

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In egg-laying hens, medullary bone serves as a reservoir of labile calcium to be used during egg shell calcification. The purpose of this study is to characterize medullary bone cell changes during the egg-laying cycle and investigate the factors which might regulate and control these events. Medullary bone osteoclasts appear to be modulating their activity but not their population during the 24 h egg cycle of the Japanese Quail. Osteoclasts are uniformly synchronized, actively resorbing bone during egg-chell calcification and are 'inactive' and lack cell surface ruffled borders during the remainder of the cycle. This uniform synchronization of cells offers a unique system to study the mechanisms of activation and inactivation of bone cells, particularly the osteoclast. It is also of interest to define the factors responsible for the regulation of calcium metabolism and bone cell changes in hens. Initial studies will center on the possible role of estrogens, androgens, vitamin D metabolites, calcitonin and possibly pituitary factors.

BIBLIOGRAPHIC REFERENCES: Rapid activation of the medullary bone osteoclast cell surface by parathyroid hormone. S. C. Miller, J. Cell Biology 76:615-618, 1978. The effect of dichloromethylene diphosphonate, a pyrophosphate analog, on bone and bone cell structure in the growing rat. S. C. Miller and W. S. S. Jee, Anat. Rec., in press, 1979.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $36,183

2.0226, BONE IN VITRO - ULTRASTRUCTURE AND AUTORADIOGRAPHY

R.S. Feldman, Harvard University, Boston Campus, Dept. of Oral Biology & Pathophysiology, *Boston, Massachusetts* 02138 (R23 DE 05332-01)

This study will investigate the activity of Parathyroid extract, Prostaglandin E2 and Phospholipase A2 on bone in mouse calvarium tissue culture. By light microscopic quantitative analysis and ultrastructural analysis, bone cells will be examined for evidence of morphologic changes due to these agents. By means of radioactive isotope localization, it will be possible to quantitate the kinetics of osteoclast augmentation by mononucleated cells in bone resorption in vitro, and alterations in the metabolism of bone forming cells in bone remodeling in vitro.

Parathyroid extract induces bone resorption in vitro, and Prostaglandin E2 and Phospholipase A2 enhance resorption in various bone systems. Parathyroid acts on the cellular level to inhibit the formation of new bone and to induce the formation of osteoclasts, the cell responsible for the pathologic bone loss in chronic destructive periodontal disease. Prostaglandin, a local or cellular hormone, may be an important mediator or modulator of chronic inflammation and pathologic bone resorption, and seems to act in a fashion similar to parathyroid hormone. Little is known about phospholipase, which was first shown to effect bone resorption in the calvarium system.

This research is designed to present new evidence about the net bone loss seen in periodontal pathology.

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National Inst. of Health,
National Inst. of Dental
Research $17,150

2.0227, PROSTAGLANDINS AND THROMBOXANE IN PERIODONTAL DISEASES

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The biochemical aspect of the research proposal is to investigate the biosynthesis and metabolism of prostaglandins and thromboxane in gingival tissues. Preliminary studies had shown the prostaglandin E2 levels are elevated in diseased human gingiva and may, therefore, participate in the pathogenesis of peridontal disease.

Subcellular fractions of the gingival tissue obtained from patients with peridontal disease will be used for assays of the enzymes (phospholipase, PG synthetase and cyclooxygenase and thromboxane synthetase) which are intimately involved in the biosynthesis of prostaglandins and thromboxane. The endoperoxide intermediates PGG2 and PGH2 will be isolated and their biological activity evaluated. The mechanism for the formation of thromboxane A2 and hydroxy fatty acid will also be examined. In the study of prostaglandin metabolism, 14C or 3H labeled PG will be used as substrate, and the activities of the metabolic enzymes (15-OH-dehydrogenase, delta 13,14 reductase and PGE 9-ketoreductase) will be measured. The sensitivity of the PGE 15 OH-dehydrogenase and PGE 9-ketoreductase to different vasoactive peptides and steroid hormones will be given special attention.

Further investigations of the release and ultimate fate of these vasoactive lipids will then be related to the possible physiological mechanism for the regulation of the inflammatory process and bone resorption in peridontal disease.

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Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $34,882

2.0228, COLLAGENOUS MATRIX AND BONE DIFFERENTIATION

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The objective of this project is to investigate extracellular matrix-cell interactions employing an experimental system of matrix-induced endochondral bone differentiation. This experimental model further affords a method to undertake systematic studies on the biochemistry and physiology of endochondral bone formation. Subjects currently under investigation are: (1) the local mitogenic effects of collagenous bone matrix; (2) changes in proline-synthetic and degradative enzymes during matrix-induced cartilage and bone development; (3) immunofluorescent localization of type IV collagen and laminin during endochondral bone differentiation and regulation by pituitary growth hormone; (4) influence of magnesium depletion on endochondral bone formation; (5) influence of experimental diabetes and insulin on cartilage and bone differentiation; and (6) role of collagen-cross-linking in mineralization of bone.

BIBLIOGRAPHIC REFERENCES: Faltz, L.L., Reddi, A.H., Hascall, G.K., Martin, D., Pita, J., and Hascall, V.C.: Characteristics of proteoglycans extracted from the Swarm rat chondrosarcoma with associative solvents. J. Biol. Chem. 254:1375-1380, 1979. Rath, N.C. and Reddi, A.H.: Collagenous bone matrix is a local mitogen. Nature 278:855-857, 1979.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $120,836

2.0229, ELECTROMAGNETIC INSTRUMENTATION TO ACCELERATE BONE HEALING

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The recent demonstration in human patients that electromagnetic fields can assist in fracture healing is being exploited in a two phase research program directed toward specifying the engineering factors required to design practical equipment suitable for clinical evaluation in orthopaedic and dental surgery. The first phase was supported by grant 76-19469.

The first phase investigated pulse characteristics designed to stimulate bone repair with intermittent rather than continuous pulsing. Those tests used tissue culture procedures to survey a wide selection of possible pulse characteristics. These in vitro tests will be continued in the second phase.

Promising pulse regimes will be tested in two animal models. The second phase will include biological safety tests to establish that the prospective applications to reduce simple fracture repair time to half the present time will not induce side effects.

SUPPORTED BY

U.S. National Science Foundation, Directorate for Engineering & Applied Science, Div. of Applied Research	$0

2.0230, A STUDY OF BONE RESORPTION IN THE HUMAN ALVEOLAR PROCESS & MOUSE ORGAN CULTURES

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PLAN: The periosteum of mouse calvaria exposed to parathyroid extract (PTE) in vitro exhibits enhanced bone resorption and osteoclast neogenesis. 3HTdR was used as a label for determining the derivation of nuclei within PTE stimulated osteoclasts. The incorporation kinetics of mononuclear precursor cells into osteoclasts during hormonal stimulation was assayed using this technique.

PROJECT OBJECTIVES: (1) To quantitate in vitro changes in the osteoclast population of mouse calvaria during PTE-stimulated bone resorption. (2) To investigate, by means of 3HTdR autoradiography, the derivation of nuclei in periosteal cells and newly forming osteoclasts. Specific attention is being focused on the incorporation kinetics of post-mitotic mononuclear cells into osteoclasts during bone resorption.

METHOD: Quantitative histologic analysis of select areas of calvaria will be used to study osteoclast neogenesis: 3HTdR light microscopic autoradiography will be employed to identify changes in the periosteal cell population, specifically multinucleated osteoclasts.

CLINICAL RELATIONSHIP: The alveolar bone loss that characterizes human chronic destructive periodontal disease is due to osteoclastic resorption. This investigation is designed to study the early cellular events associated with this phenomenon.

SUPPORTED BY

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2.0231, HEALING OF FREEZE-TREATED MAXILLARY BONE

R.D. Marciani, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Leestown Pike, Lexington, Kentucky* 40507 (596-003-P)

Early studies suggested that the combined techniques of excision, freezing and reimplantation may provide a new avenue for the treatment of intraoral bone tumors. Previous experiences of freezing bone in situ and reimplanting freeze-treated bone were restricted to the mandible, but strongly suggested that similar procedures may be feasible in the maxilla. Ten adult monkeys were used as the experimental animals in the investigation of bone healing and revascularization associated with resected frozen and reimplanted maxillary bone. Following reflection of a full-thickness buccal and palatal mucoperiosteal flap, hemimaxillectomies were performed on all ten animals. Five of the hemimaxillas were placed into liquid nitrogen for ten minutes and allowed to thaw to bench temperature. The remaining five hemimaxillas were allowed to sit in the open environment for thirty minutes. All the hemimaxilla were reimplanted, wired into their former position and the mucoperiosteal flaps were repositioned and sutured. The animals were sacrificed in pairs at three weeks, six weeks, three months, and six months (the one year animals remain to be sacrificed). The process of revascularization and bone healing was studied by means of a microangiographic technique. All the animals sacrificed showed complete healing and reconstitution of the resected and reimplanted hemimaxilla. Evaluation of the microangiograms and histologic sections is now in progress.

SUPPORTED BY

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2.0232, HUMAN ILIAC ALLOGRAFTS IN PERIODONTAL OSSEOUS DEFECTS

R.G. Schallhorn, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *1055 Clermont St., Denver, Colorado* 80210 (554-001-P)

Animal and human studies have continued on the correction of periodontal osseous defects via grafting of allogeneic cancellous bone and marrow (ACBM). Additional data on long term stability has been accumulated in initially successfully treated ACBM sites. New disease, foreign body impaction, failure to follow the prescribed periodontal maintenance program, and atypical acute periodontitis have been observed in a small percent of cases. Also new or recurrent disease has been observed in patients that have undergone major stress situations implicating a hormonal basis of response. Studies are currently projected to explore the effect of elevated cortisol levels on healed new attachment sites. Additional histologic specimens have been obtained on both graft and non-graft new-attachment sites in humans. Evaluation of 100 specimens have shown new bone in 85% of the grafts treated versus 33% of the nongraft sites. Cementogenesis was found to occur in 86% of the graft treated versus 33% of the non-graft sites demonstrating a marked enhancement of favorable repair with osseous grafts. Human root preparation studies have continued and have demonstrated a low density of crystallites found associated with individual collagenous fibrils and bundles of fibrils in diseased cementum and spaces devoid of crystallites suggesting microchannels. Project continues.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery funds n.a.

2.0233, THE ROLE OF ZINC IN BONE METABOLISM

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The project 'The Role of Zinc in Bone Metabolism' is in progress. During the year the following resulted from work on the project: 1. paper 'Loss of Zinc From Bone During Deficiency State' Nutrition Reports International Vol. 17, No. 3 March 1978; 2. another study in which rats were fed a 20 or 40 percent protein diet, they showed an increased urine acid, zinc and calcium excretion. In addition, there was an increased concentration of zinc in the bones of the animals. The project is to be continued. A study is planned to determine if a state of zinc deficiency in animals will lower the increased concentration of zinc in bone caused by a high protein diet.

SUPPORTED BY

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2.0234, AN IN VITRO RESEARCH STUDY IN THE ROLE OF TRACE ELEMENTS IN TRAUMATIC INJURIES TO OSSEOUS TISSUES

J.J. Dooner, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Leavenworth, Kansas* 66048 (686-005-P)

Three additional experiments were started in June-August of 1977. All explants used were legs and all were experimentally fractured. The medium used was Waymouths MB752/1 supplemented with 200 mg/100 ml of glucose, 30 mg/100 ml of ascorbic acid, 0.045 mg/100 ml of ferrous sulfate, and 1 ml/100 ml of antibiotic/antimycotic mixture. The medium for the zinc-treated explants also contained 0.005 mg/liter of ZNS04. All of the explants were experimentally fractured by partially cutting through the shaft of the leg and approximating the cut ends before adding the medium of the organ culture flasks. Specimens were cultured 2, 4, 7 or 9 days. The medium was replaced every 2-3 days. One-half of the explants were fixed in formalin and for paraffin embedding and histological examination of hematoxylin and eosin-stained sections. The other half of the paired specimens were immediately frozen and held for analysis for zinc-uptake by atomic absorption spectrophotometosy. At the present time all sectioning is completed. The atomic absorption analysis is currently in progress. All work that was previously in progress has been completed.

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2.0235, EFFECTS OF TRACE ELEMENTS ON BONE FRACTURE REPAIR IN VITRO

J.J. Dooner, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Leavenworth, Kansas* 66048 (686-006-I)

The study of the effect of zinc on bone fracture repair has been completed. A total of 193 specimens from 17-18 day old fetal rats were examined. Histologic evaluation was done on 97 of the specimens and 96 specimens were analyzed for zinc content by atomic absorption spectrophotometry. The histologic specimens were examined for periosteal activity in long-bone explants and connective tissue activity in mandibular explants. Bone matrix formation was evaluated in all explants. In the early stage of the experiments (2-4 days in vitro) more periosteal activity was noted in zinc-supplemented explants than in non-zinc explants. After 4 days in vitro, the zinc-supplemented explants showed a higher connective tissue activity, in mandibular explants, than in the non-zinc explants. Both of these results--an immediate increase in periosteal activity in long-bone explants--appear to indicate increased cellular activity due to the addition of 0.005 ppm zinc to the medium. The effect of zinc on bone matrix formation and bone repair was not conclusive because: (1) the length of time chosen for the experimental period may not have been sufficient to allow for complete repair and (2) some of the fractured explants were physically displaced which did not allow repair. However, repair of some fractures by connective tissue and/or bone did occur in zinc-supplemented explants which indicates a positive effect of zinc on bone repair. No differences were noted in the zinc-supplemented and non-zinc explanted when they were analyzed for zinc by atomic absorption spectrophotometry. This contrasts with previous results where increases in zinc content were noted in zinc-supplemented explants.

The study of the effect of manganese on bone repair in vitro has not been completed.

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2.0236, THE EFFECT OF BACTERIAL COMPONENTS ON BONE RESORPTION

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OBJECTIVE: Investigation of the relationship of dental bacterial plaque components and alveolar bone resorption in periodontal disease.

APPROACH: Bone resorption is assessed by an in vitro assay using 45Ca labelled rat fetal long bones maintained in culture. Extracts of specific fractions of oral bacteria and defined dental plaque are prepared and their direct and indirect actions on bone resorption investigated. The degree of in vivo bone loss associated with the defined plaque is assessed radiographically. Attempts will be made to correlate the in vivo and in vitro effects of lipoteichoic and endotoxin(s) on bone resorption.

PROGRESS: Lipoteichoic extracted from actinomyces viscosus stimulates bone resorption in vitro.

SUPPORTED BY

University of London	funds n.a.

2.0237, HUMAN GINGIVAL LYSOSOMES IN VIVO AND IN VITRO

G.G. Rose, University of Texas, Health Science Center at Houston, Dental Branch, Dept. of Medicine, *6515 Freeman, Houston, Texas* 77025 (R01 DE 04337-03)

Human gingival biopsies from pathological-nonpathological sources are used to establish fibroblast cell lines for in vitro analysis and electron microscopic study. The principal objectives are to develop clear interpretations on the biological mechanisms of function and response for human gingival cells and to detect new knowledge about their lysosomal complexes. In particular, the studies are relative to the fibroblast's role in synthesizing, degrading, and remodelling collagen matrices and their response to biological and foreign agents of disease processes.

BIBLIOGRAPHIC REFERENCES: Rose, G.G., Yajima, T., and Mahan, C.J.: Microscopic Assay for the Phagocytotic-Collagenolytic Performance (PCP Index) of Human Gingival Fibroblasts In Vitro, Journal of Dental Research, in press, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$30,913

2.0238, COLLAGENOLYTIC ACTIVITY IN PERIODONTAL DISEASE

J.W. Simpson, University of Texas, Health Science Center at Houston, Dental Branch, Dept. of Dental Science, *6515 Freeman, Houston, Texas* 77025 (R01 DE 04485-03)

The proposed investigation is directed toward the study of collagen loss during periodontal disease due to collagenase activity. Specifically, a number of agents and several cell types will be tested for their ability to induce active collagenase in cultured cells. Agents to be tested will include plaque extracts, Dilantin sodium, dexamethasone, thyroxine, parathormone, prostaglandins and endotoxin. Cell types to be tested include T lymphocytes, B lymphocytes and mast cells. Cells to be cultured include gingival fibroblasts and pulmonary macrophages. Experiments will be conducted to determine whether the appearance of active collagenase in cell cultures results from the induction of collagenase. Another series of studies will be carried out to purify and characterize the collagenase inhibitor found in the culture media of gingival fibroblasts.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0239, TRANSGLUTAMINASES - SPECIFICITIES, PHYSIOLOGICAL FUNCTIONS AND CATABOLISM OF PRODUCTS

J.E. Folk, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Enzyme Chemistry Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00001-28 LB)

Specificity studies on transglutaminases using synthetic model substrates are underway. The relationship to cellular control processes and other biological processes of polyamine-protein conjugates produced by these enzymes in cells and body fluids is under investigation. Knowledge of the catabolism of these conjugates has been obtained.

BIBLIOGRAPHIC REFERENCES: Schrode, J., and Folk, J.E.: Transglutaminase-catalyzed crosslinking through Diamines and Polyamines. J. Biol.

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Chem. 253, 1978. Schrode, J., and Folk, J.E.: Stereochemical aspects of amine substrate attachment to acyl intermediates of transglutaminases. J. Biol. Chem. 254:653-661, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$206,260

2.0240, PHYSIOLOGICAL ROLE AND METABOLISM OF TRANSGLUTAMINASES

S.I. Chung, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Protein Chemistry Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00049-08 LB)

The physiological function and the mode of regulation of the transglutaminases are being studied. The roles of individual transglutaminases in the formation of cellular membranes, in membrane-mediated stimulation of specific cellular function, and in the regulation of tissue matrix stabilization following injury are under investigation.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$73,694

2.0241, GINGIVAL OXIDATIVE METABOLISM DURING WOUND HEALING

A.S. Fine, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Research Laboratory, *1st Ave. at E. 24th St., New York, New York* 10010 (630-001-P)

Previously we reported that gingival injury activated cAMP, and DNA levels in a cyclic manner, at the gingival wound, distal contralateral (gingival) and palate wound peripheral non-injured sites, (J. Dent. Res. 57, Abstract 670, 1978). Current investigation is directed towards the (1) Em localization of adenylate cyclase in normal gingiva and at gingival wound and distal sites as a function of time after injury, (2) biochemical analysis of adenylate cyclase in total homogenates, plasma membrane, and mitochondrial fractions in control, wound, and distally activated gingival, and palate sites as a function of time after injury.

In this context we wish to report upon the EM localization of adenylate cyclase activity in the epithelial and dermal compartments of normal control rat gingiva. Adenylate cyclase activity was found to occur in all epithelial cells, below the keratin layer, and within the dermal (fibroblast) compartment, in gingiva which was incubated with adenyl-iododiphosphate (AMP-PNP) and stimulated by the addition of F1-, histamine, and epinephrine. Adenylate cyclase localization was found primarily with the epithelial and fibroblast mitochondria in intact gingiva. Analysis of adenylate cyclase (EM localization) in isolated gingival mitochondria also revealed the presence of reaction production within the mitochondrial matrices. Our data suggests that mitochondrial adenylate cyclase may play a role in modulating cellular events in both epithelial and fibroblast cells.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0242, THE BIOLOGY OF THE PERIODONTIUM IN HEALTH AND DISEASE

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Research on the biology of the periodontium of various primate species from man to marmosets will be performed in a coordinated multidisciplinary program. The target is the control of human periodontal disease through an understanding of the basic disease processes. The basic objective of the program-project is the study of the periodontium as a biological unit in health and disease. Multidisciplinary and interdisciplinary experiments are designed to elicit the responsiveness of the periodontium to changes in its biological environment. A three-pronged interdisciplinary attack on the problems of periodontal disease, designed to estabish the manner in which (I) environmental factors, (II) conditioning factors and (III) mediating factors interact to produce inflammatory periodontal disease in men and other primates has been developed. Thus, a solution to the complex health problem, periodontal disease, is being sought through coordinated research on multiple and interdisciplinary aspects of the problem. The effectiveness of the program is critically dependent upon the contribution of each member of the research team. The disciplines represented are: bacteriology, biochemistry, electron microscopy, histology, immunology, immunopathology, nutrition, oral physiology and virology.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health,

National Inst. of Dental Research	$0

2.0243, KERATOHYALIN IN KERATINIZATION OF ORAL MUCOSA AND SKIN

B. Dale, University of Washington, School of Dentistry, Dept. of Periodontics, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P50 DE 02600-130032)

Keratinization of oral mucosa and skin results in the protective layer called the stratus corneum, covering the body and parts of the oral cavity. Cells of the stratum corneum contain keratin filaments and the stratum corneum basic protein, SCBP, the possible interfilamentous matrix protein. Biochemical and immunologic evidence suggests that SCBP is derived from a precursor protein in keratohyalin granules, which has a higher molecular weight than the product. Keratin filaments aggregate with the SCBP in vitro, but not with keratohyalin preparations, to form fibers or macrofibrils with highly aligned filaments. Our hypothesis is that the SCBP is generated from the precursor by a specific protease, and then associates with keratin filaments forming a macromolecular complex. These events occur at the time of conversion of cells of the granular layer to those of the s. corneum. This hypothesis will be tested by isolating the precursor from newborn rat epidermis, by investigating the mechanism of formation of SCBP from its precursor, and by studying the interactions of SCBP and keratin filaments from epidermis, and from keratinized, parakeratinized, and non-keratinized human oral mucosa. The role of SCBP in human oral mucosa will be assessed by correlating its presence with the type of keratinization in normal tissue and with the extent of inflammation in gingiva.

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2.0244, MULTICOMPONENT POLYMER SYSTEMS

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The objective is to prepare novel multicomponent bipolymer systems which greatly improve and extend the range of biomaterials used in health care applications. These biomaterials will have improved processing characteristics, strength, and biocompatibility. For example, a deficiency of existing acrylic bone cements is that during polymerization they reach a peak temperature which is sufficiently high to cause thermal trauma to adjacent biological tissue. In this case the objective is to limit this temperature in a controlled way by inclusion of a crystalline polymeric additive without compromising other properties such as mechanical strength and biocompatibility. In the case of acrylic denture base materials this same principle can be applied with the objective of rigorous control of porosity, and hence strength, even in thick sections in which heat build-up would otherwise cause problems.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$28,137

2.0245, PRIMARY STRUCTURE OF PROTEINS IMPORTANT IN INTERMEDIARY METABOLISM, HEMOSTASIS AND ORAL BIOLOGY

H.S. Kingdon, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Periodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130152)

The objective of this project is to determine the primary structure of a large number of proteins involved in hemostasis, and to correlate their primary structures with the function they play in hemostasis. The primary structures are being determined by techniques in which the proteins are subjected to selected enzymatic digestion, the peptides are purified by ion exchange chromatography, and then their sequences are determined in an automated protein-peptide sequencer. The residues formed in the automated Edman degradation in the sequencer are identified by gas liquid chromatography, thin-layer chromatography, and high-pressure liquid chromatography.

In collaboration with others at the Dental Research Center and elsewhere, we also determining the primary structure of other proteins of interest in hemostasis in oral biology, or in general in regulation of metabolism. The proteins under study include human thrombin, ribonuclease and deoxyribonuclease from bovine parotid rabbit and bovine gland, bovine Factor XIa, and E. coli glutamine synthetase and collagen.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,

National Inst. of Health,
National Inst. of Dental
Research $73,742

2.0246, BIOCHEMICAL MECHANISMS RELEVANT TO DENTISTRY

M. Caplow, University of North Carolina, Chapel Hill Campus, School of Medicine, Dept. of Biochemistry, *Manning Dr., Chapel Hill, North Carolina* 27514 (R01 DE 03246-10)

Research is concentrated in two areas: (a) Dextran formation by cariogenic microorganism (Strep mutans) is under study. Enzymes involved in the synthesis of water soluble and water insoluble dextran are purified, and mechanistic study involving kinetic analysis is carried out. (b) The role of guanine nucleotides in microtubule assembly is evaluated in kinetic studies of microtubule assembly, special attention is given to an analysis of the role of the proteins other than tubulin.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $70,665

2.0247, STRUCTURAL-FUNCTIONAL CHANGES IN FREEZING ORAL TISSUE

J.R. Natiella, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Pathology, *3435 Main St., Buffalo, New York* 14214 (R01 DE 03991-05)

This project deals with the application of liquid nitrogen freezing to several body sites in the primate. A base line study of the repair and regeneration of palate, mandible, buccal mucosa, tongue, parotid, submandibular gland, and skin is devised assessing the effects of spray and probe freezing at selected temperatures. The evaluation is by light and electron microscopy.

BIBLIOGRAPHIC REFERENCES: Meenaghan, M.A., Natiella J.R. and Gage, A.A. The Effects of therapeutic freezing on pigmented mucosa and skin. Anatomical Record, 190(2):616, 1978.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $43,827

2.0248, EFFECT OF FLUORIDE ON CAMP AND GLUCOSE METABOLISM

D.W. Allmann, Indiana University, Indiana University - Purdue University at Indianapolis, School of Medicine, Dept. of Biochemistry, *1219 W. Michigan St., Indianapolis, Indiana* 46202 (R01 DE 04387-03)

It is proposed to continue our investigations of how inorganic fluoride alters the production of cAMP in various tissues and how fluoride alters glucose metabolism in the intact liver cell. At present we have shown that feeding young rats a fluoride-free diet (less than 0.05 ppm fluoride) and 1 ppm fluoride in the drinking water results in significant increases, compared to rats receiving a fluoride-deficient diet, in the cAMP levels in urine, liver, mandibular gland, tibia, femur, kidney, lung and heart within four weeks. Also that there are changes in the concentration of some of the glycolytic intermediates. There is a significant decrease in 2-phosphoglycerate, 3-phosphoglycerate, pyruvate, and lactate and an increase in phosphoenolpyruvate in the liver of rats fed fluoridated water (1 ppm) compared to rats fed a fluoride-deficient diet. These results suggest that two effects of NaF are an increase in adenylate cyclase activity and a decrease in enolase activity. We plan to extend this study to include the effect of other inorganic fluoride salts, e.g., Na2PO2F, Na2SiF6 and shorter time periods.

We also are examining the effects of NaF and Na2PO3F on the production of cAMP, glucose, pyruvate and lactate in hepatocytes isolated from fed and fasted rats. At present we are able to demonstrate that NaF alters the production of the metabolites mentioned above. In general, the inorganic fluoride salts alter liver cell metabolism in s similar manner to that of glucagon.

BIBLIOGRAPHIC REFERENCES: Allmann, D.W., Miller, A., and Shahed, A.R., Effect of NaF on Glycolysis and Cyclic-AMP Production in Isolated Rat Hepatocytes. Fed. Proc. 37, 1689 (1978). Allmann, D.W., Miller, A., and Kleiner, H. S., Effect of Fluoridated Water on 3'5'-Cyclic AMP Levels in Various Rat Tissues. J. Dent. Res. 57, June, 1978, in press.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $42,478

2.0249, MINERAL NUTRITION AND ALVEOLAR BONE LOSS

H.H. Messer, University of Minnesota, Minneapolis Campus, School of Dentistry, Dept. of Oral Biology, *6 Morrill Hall, Minneapolis, Minnesota* 55455 (R01 DE 04475-02)

The objectives of the study are: 1) to determine whether alveolar bone loss is influenced by changes in mineral metabolism, 2) to compare changes in alveolar bone with those occurring in other parts of the skeleton, 3) to investigate the underlying metabolic changes accompanying alveolar bone loss. The study will use two strains of mice, one known to be susceptible to severe alveolar bone loss (STR/N) and one resistant to alveolar bone loss (random bred Swiss-Webster strain). Dietary Ca:P ratios will be varied in the range 1:1 to 1:4 at two levels of calcium in the diet, 0.1% (Ca deficient) and 0.6% (adequate Ca). In a separate study, the zinc level of the diet will be varied from adequate (20-25 ppm) to marginally deficient (5-10 ppm). Alveolar bone loss will be quantitated by direct measurement, and histometrically in the interradicular area of the low second molar. Metabolic changes will be assessed by measurement of mineral content, lysosomal enzyme levels, and by acid production in bone culture. Changes in alveolar bone will be compared with changes in the femur on the basis of rapidity of onset, severity of bone loss, and extent of change in metabolic patterns.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$49,287

2.0250, PERIODONTAL DISEASE AND COPPER AND ZINC METABOLISM

R.J. Cousins, Rutgers the State University of New Jersey, New Brunswick Campus, Undergraduate School, Dept. of Nutrition, *Old Queens Bldg., New Brunswick, New Jersey* 08903 (R01 DE 04606-02)

The severity of human periodontal disease has been directly correlated to the serum copper concentration. A model system, using both rice rats and hamsters, and which utilizes graded, controlled-intake levels of dietary copper will be employed to evaluate the influence of this nutrient on the development of experimental periodontal disease. Hepatic copper mobilization and the activity of specific metalloenzymes, ceruloplasmin, lysyloxidase, superoxide dismutase and cytochrome oxidase will be correlated with dietary copper and periodontal lesions. The influence of dietary zinc, calcium and phosphorus will also be investigated.

Copper metabolism in the oral tissues will be investigated in vivo and in vitro. The role of bacterial endotoxins, leukocytic endogenous mediator and antibiotics in the uptake and function of 67Cu and 67Cu-ceruloplasmin will be investigated in vitro using gingival tissues from normal animals and those exhibiting signs of periodontal disease. These experiments will attempt to define the role of copper in periodontal disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$48,903

2.0251, PATHOGENESIS OF BONE LOSS IN PERIODONTAL DISEASE

B.R. Rifkin, University of Rochester, School of Medicine & Dentistry, Dept. of Pathology, *601 Elmwood Ave., Rochester, New York* 14627 (R23 DE 04443-03)

The effects of inflammation on bone cells are not well understood. The work in progress in our laboratory is designed to help elucidate the mechanisms involved in bone loss caused by an inflammatory infiltrate. Our studies involve an ultrastructural examination of two animal models of periodontal disease, and culture fetal long bones stimulated to resorb by prostaglandin and osteoclast-activating factor. The effects of these agents on isolated bone cells are also being examined.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0252, EFFECTS OF ELECTROSURGERY UPON THE GINGIVAL ATTACHMENT TO THE TEETH

J.R. Blankenship, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *2215 Fuller Rd., Ann Arbor, Michigan* 48105 (506-002-F)

Various electrosurgical instruments are often used to facilitate impression techniques as part of operative and restorative dentistry. It has been assumed that these procedures are harmless to the periodontium on a long term basis in that no periodontal support is lost. However, this hypothesis has never been tested under controlled conditions, and a recent paper by Glickman and Imber reported that gingival electrosurgery could result in extensive loss of gingival attachment to the teeth. Thus, the purpose of this study was to test in monkeys whether electrosurgery as often used in restorative dentistry is a distinct possibility that may produce harmful effects.

This study has been completed. The results were published in the Journal of Periodontology and as a Thesis. Conclusions from the study were: 1. Electrosurgical troughing involves incision into connective tissue. 2. Troughing is apt to cause slight gingival recession and apical positioning of the soft tissue attachment. 3. Contact of the cementum with the activated electrosurgical tip will cause an alteration, probably a burn, in the cementum.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery — funds n.a.

2.0253, CONNECTIVE TISSUE ATTACHMENT TO ROOT SURFACES IN VITRO

P.L. Walters, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Periodontology Service, *Leavenworth, Kansas* 66048 (686-002-P)

Having difficulty growing fibroblasts (gingiva) without a CO2 incubator. Am waiting for CO2 incubator to enhance growth of fibroblasts.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery — funds n.a.

2.0254, UTILIZATION OF TETRACYCLINE IN WOUND HEALING - CITRIC ACID USED IN DOGS - IN VITRO USE OF CITRIC ACID ON HUMAN TEETH

P.L. Walters, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Periodontology Service, *Leavenworth, Kansas* 66048 (686-003-I)

Attempting to grow strain of Fibroblast to determine the effect of citric acid upon the root surface, demineralized and possible removal of endo and exo toxins.

Utilization of dogs infrabony defects are created and maintained for two months with copper bands cemented with ZOE. The bands are then removed and these lesions are allowed to become chronic, after which they are surgically treated with a routine flap. At this time citric acid is placed directly upon (1) unscaled cementum, and (2) scaled root. The control is saline. (Time of application two minutes).

Tetracycline from capsule form is placed directly under the flap in dogs and varying time schedules of healing are evaluated.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery — funds n.a.

2.0255, THE ROLE OF LIPOPROTEINS IN MICROBIAL CALCIFICATION

B.D. Boyan Salyers, University of Texas, Health Science Center at Houston, Dental Branch, Dept. of Microbiology, *6515 Freeman, Houston, Texas* 77025 (R01 DE 04212-05)

Microbial calcification has proven to be a useful model for studying biologic mineral formation. The mineral species formed by Bacterionema matruchotii is crystallographically indistinguishable from biologic apatite of bones and teeth. The calcification nucleator of B. matruchotii has been identified as proteolipid: basic, hydrophobic protein complexed with acidic phospholipid. Calcifiable proteolipid has been isolated from marmoset bone and human dental calculus. A within-strain comparison of B. matruchotii and a variant exhibiting impaired calcifiability has provided insight into cellular regulation of calcification. A record of the process of mineral formation in the organism provides a baseline for further studies.

The purpose of the proposed research is to define the mechanism of intracellular apatite deposition in B. matruchotii through continued characterization of the nucleating entity, metabolic studies and examination of the process of apatite formation. Cellular regulation of calcification will be investigated by examining the interaction of calcifiable proteolipid with cell membrane components and through comparative studies with other mircoorganisms. Methodology developed for the microbial system can then be applied to vertebrate mineral formation.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research — $33,435

2.0256, THE EFFECTS OF CITRIC ACID ON CEMENTUM AND DENTIN

P.L. Walters, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Periodontology Service, *Leavenworth, Kansas* 66048 (686-001-P)

Mongrel dogs are to be used for this study to determine if citric acid can accelerate new attachment of connective tissue to the tooth. Each dog, under general anesthesia, will have 2 walled infra-bony defects created adjacent to maxillary and mandibular teeth. Copper bands with ZOE wll be fitted over each tooth. Each band will extend into the defect. Two months of healing will occur and then the bands will be removed. Two more months of healing will occur and then the chronic periodontal defects will be treated in one of four ways: 1. Citric acid on cementum; 2. Saline on Cementum; 3. Citric acid on dentin; 4. Saline on dentin. Treatments are applied at varying times (5 to 30 days). The dogs will be sacrificed and the jaws submitted for H&E light microscopy.

Preliminary work indicates that citric acid may increase the rate at which a connective tissue new attachment will be formed.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

PATHOLOGY - MISCELLANEOUS

2.0257, SURFACE RECEPTORS ON PLAQUE FORMING ORGANISMS

B. Rosan, University of Pennsylvania, School of Dental Medicine, Dept. of Microbiology, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (P50 DE 02623-120014)

Streptococcus sanguis and S. mitis constitute major bacterial components of early dental plaque. These organisms appear to react specifically with salivary glycoproteins. In addition, S. sanguis has been shown to interact with other plaque bacteria, i.e., Actinomyces viscosus and Bacterionema matrochutii. Both these kinds of reactions are thought to involve specific bacterial surface receptors. The purpose of our studies is to define the polymers which comprise these receptors. In order to accomplish these objectives, we will employ an adherence assay utilizing hydroxyapatite beads coated with saliva. It has been observed that attachment of S. sanguis and other oral organisms to these beads follows the Langmuir Adsorption Isotherm which is derived from the Law of Mass Action. Thus, it is possible to calculate both an affinity constant (Ka) and the number of binding sites available for attachment (N). The product, KaN, is a useful index for comparing the ability of various strains to adhere in the in vitro model. Studies have already shown differences in adherence between the various serotypes of S. sanguis as well as among other species of oral streptococci. Competition assays have been developed which suggest at least four different types of receptors may be involved in adherence among these organisms. Studies are now underway which seek to define these receptors. In addition to adherence studies, we are progressing on the in vitro assay for 'corn cobs' using B. matrochutii and serotype 1 strains of S. sanguis. These preliminary studies are directed at determining optimal conditions for corn cob formation.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$111,878

2.0258, PROSTAGLANDINS, CYCLIC AMP AND STEROIDS IN GINGIVA

T.M. ElAttar, University of Missouri, Kansas City Campus, School of Dentistry, Dept. of Biochemistry, *10th & Troost Sts., Kansas City, Missouri* 64110 (R01 DE 04276-03)

Our interest has been directed towards the relationship between prostaglandins and cyclic AMP in gingival tissues of patients with periodontal disease and the effect of various hormones on the synthesis of these compounds.

The overall objectives of the total project are: (1) To determine the levels of prostaglandins and cylic AMP in healthy and diseased human gingiva (chronic periodontitis), 0(2) To study the effect of glandular hormones (steroid-parathyroid hormone-thyroid hormone-calcitonin-epinephrine) on the synthesis of prostaglandins and cyclic AMP in human gingival tissue, (3) To study the effect of inflammatory tissue hormones (histamine-bradykinin) on the synthesis of prostaglandins and cyclic AMP in the gingiva, (4) To study the effect of prostaglandin inhibitors on the synthesis of prostaglandins in the gingiva.

BIBLIOGRAPHIC REFERENCES: ELAttar, T.M.A. & Lin, H.S. (1978a). Prostaglandins and cyclic AMP in human gingiva with periodontal disease. In Mechanisms of localized bone loss. Editors, J.E. Horton, T.M. Tarply and F.W. Davis. Information Retrieval Inc., Washington D.C. and London. ELAttar, T.M.A. and Lin, H.S. (1978b). Cyclic AMP as mediator of prostaglandin effects in human gingiva. Journal of Dental Research 57 (Special Issue A), 313.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$65,438

2.0259, THE STRUCTURE AND FUNCTION OF PERIODONTAL TISSUES AND THE MASTICATORY MECHANISM

Unknown, Medical Research Council, Dental Unit, ***Bristol, England, United Kingdom***

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$66,924

DIAGNOSIS & TREATMENT

2.0260, ROLE OF PRESSURIZED WATER LAVAGE IN THE PRACTICE OF MILITARY DENTISTRY

A. Gross, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Basic Sciences, *Washington, District of Columbia* 20012 (DA0H6036)

To determine the efficacy and application of pressurized water lavage to the treatment and prevention of disease in traumatic wounds, oral maxillofacial surgery and military dentistry.

Specially designed instruments which yield water jets at different pressures and in both pulsating and nonpulsating streams are being used to study the effect of this modality on wound healing, dental plaque, and bacterial populations. The target tissue pressures with various water jet devices will be examined. The applicability to presurgical hand cleansing is being investigated.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research	funds n.a.

2.0261, PERIODONTAL DISEASE IN PATIENTS WITH IMMUNE DISORDERS

B.M. Levy, University of Texas, Health Science Center at Houston, Dental Branch, Dept. of Pathology, *6515 Freeman, Houston, Texas* 77025 (N01DE52454 (CONTRACT))

The contractor proposes to study a minimum of 25 patients with known deficiencies of the immune system and their state of periodontal health shall be documented to determine if there is any correlation between these two phenomena. The contractor will characterize in detail the immune deficiencies through assay of cellular immune reponse, as well as inflammatory response, and to characterize the clinical periodontal disease entity according to currently acceptable periodontal disease indices.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0262, PERIODONTAL DISEASE IN PATIENTS WITH IMMUNE DISORDERS

H.R. Creamer, Oregon State Higher Education System, University of Oregon Health Sciences Center, School of Dentistry, Dept. of Microbiology, *611 S.W. Campus Dr., Portland, Oregon* 97201 (N01DE52455 (CONTRACT))

The contractor proposes to study a minimum of 25 patients with known deficiencies of the immune system and their state of periodontal health shall be documented to determine if there is any correlation between these two phenomena. The contractor will characterize in detail the immune deficiencies through assay of cellular immune reponse, as well as inflammatory response, and to characterize the clinical periodontal disease entity according to currently acceptable periodontal disease indices.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0263, BASIC STUDIES BEARING ON PERIODONTAL DISEASE

H.A. Zander, Eastman Dental Center, Dept. of Periodontology, *800 Main St. E., Rochester, New York* 14603 (P01 DE 01648-15)

Bilateral identical periodontal pockets have been produced on contralateral tooth surfaces in rhesus monkeys. On one side the pockets were treated by either (1) open curettage (four animals),(2) apically positioned flap with osseous surgery (four animals), and (3) autogenous red marrow and cancellous bone transplants (four animals). The contralateral pockets remained as untreated controls. One half of the animals in each group (i.e., two animals) will be killed at one year after operation. Specimens will be processed by standard histometric techniques and subject to histometric analysis. This will permit comparison of efficacy of treatment procedures. The remaining animals will be killed three years after the date of operation. As soon as eight additional rhesus monkeys have periodontal pockets of adequate depth, different therapeutic procedures for pocket elimination will be studied. The design of the investigations will be the same as described above.

The squirrel monkey model for marginal periodontitis will be used to assess histometrically whether simultaneous initiation of repetitive trauma and periodontitis results in loss of connective tissue and crestal alveolar bone greater than that in our previous studies. Knowing that the two etiologic factors, namely, plaque formation and jiggling, are responsible for connective tissue and alveolar bone loss we will study the ability of the periodontal structures to repair when one or both of these etiologic factors are removed.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

2.0264, REATTACHMENT OF PERIODONTAL TISSUES FOLLOWING THERAPY

S.P. Ramfjord, University of Michigan, Ann Arbor Campus, School of Dentistry, *Ann Arbor, Michigan* 48104 (P50 DE 02731-130033)

The main objective of the Epidemiology and Clinical Trial Section is to establish through clinical trials which therapeutic modality provides the best short- and long-term results in treatment of periodontal disease. Experimental animals also are used to study the biologic and histologic responses to the treatment procedures used in the clinical trials.

One hundred patients and 24 beagle dogs have been treated, and the initial clinical findings are: reduction in pocket depth and gain of attachment to an increasing extent with increasing original pocket depth both in patients and in the dogs.

Bacteriological studies in the dogs indicate a significant decrease in the preparation of anaerobic to aerobic bacteria in successfully treated pockets. If this holds true for humans, simple bacteriological tests may be developed for assessment of success in periodontal therapy.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$167,480

2.0265, INVESTIGATION OF METHODS FOR DIAGNOSIS AND TREATMENT OF DESTRUCTIVE PERIODONTAL DISEASES

S.S. Socransky, Forsyth Dental Center, Dept. of Periodontology, *140 Fenway St., Boston, Massachusetts* 02115 (P50 DE 04881-030001)

The clinical investigation of patients with destructive periodontal disease is part of a unified study of the interactions between host and microbial factors which underlie the disease process. The first series of studies will investigate longitudinal changes in untreated patients. Patients will be monitored by clinical indices, attachment level measurements, and radiographic techniques. The rate and localization of destruction in individual sites will be assessed and compared with changes in the clinical parameters. These changes will be evaluated in relationship to alterations of the microbial flora and changes in the host response.

The effect of therapeutic procedures including mechanical debridement and antiseptic or antibiotic agents on clinical parameters of disease and microbial populations will be assessed. As part of the evaluation procedure, the reproducibility of a spectrum of clinical measurements will be determined as well as their relationship to destruction of bone or the attachment apparatus. In order to extend diagnostic capabilities, more sensitive methods of clinical measurement will be developed and laboratory techniques for diagnosis of disease will be evaluated.

Early results of longitudinal studies of untreated patients demonstrated that destruction does not take place at equal rates in all periodontal lesions, but is highly localized. In certain instances, localized bone loss at rates of greater than 1 mm in 3 months have been detected in individual sites. To date, the standardized radiograph has been the most sensitive and reproducible clinical measurement of destruction.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$131,916

2.0266, MICROBIOLOGY (HUMAN)

R.J. Genco, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (P50 DE 04898-030001)

SPECIFIC AIMS: A. To enumerate the predominant flora in periodontal pockets of patients with periodontitis and juvenile periodontitis (periodontosis). B. To develop methods for rapid identification and enumeration of pocket organisms with pathogenic potential by immunofluorescence, cultural and functional procedures. C. To determine the antibiotic sensitivity of the predominant flora and of the potentially periodontopathologic flora in periodontal pockets as an aid in the selection of appropriate antibiotics for therapy. D. To monitor changes in pocket flora with therapy as part of longitudinal studies of effectiveness of therapy over a long period of time. E. To monitor development of antibiotic resistance in the oral flora during antibiotic therapy.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $124,224

2.0267, PLAQUE CONTROL - HEALING FOLLOWING PERIODONTAL SURGERY

J.T. Lindhe, Goteborgs Universitet, *411 Vasaparken, S40010 Goteborg, Sweden* (R01 DE 04890-01)

The aim of the proprosed research is to study the healing capacity of the periodontal tissues following surgery. Attempts will be made to assess the efficiency of chemical and mechanical plaque contol measures to ensure proper condititions for periodontal tissue healing. An analysis will be performed to evaluate if it is possible to restrict periodontal treatment to scaling and root planning and still obtain attachment gain and bone regeneration in infrabony defects.

All patients participating in this trial are 30-50 years of age and exhibit signs of advanced marginal periodontitis. They will be subjected to surgical pocket elimination a.m. Widman combined with scaling and root planing or to scaling and root planing only. Following treatment the patient will be maintained on preventive programs which involve either chemical or mechanical plaque control measures.

Treatment results will be assessed following clinical, radiographical examinations carried out after 6 and 24 months.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $74,636

2.0268, COMPARISON OF TREATMENT PROCEDURES USED IN ENDODONTICS

W.R. Opderbeck, College of Medicine & Dentistry of New Jersey, New Jersey Dental School, School of Dentistry, Dept. of Endodontics, *100 Bergen St., Newark, New Jersey* 07103 (R23 DE 04335-03)

During the past several years, there has been a significant increase in the use of the one visit procedure (N2) for the treatment of endodontic patients by dental practitioners in the United States. Based on scientific evidence, the N2 method is not taught in any dental school in the U.S. However, the evidence available is difficult to interpret since there is an obvious absence in the literature of studies that directly compare the N2 method with the method accepted in the United States.

The study proposed here will evaluate each method by a direct comparison of three critical aspects of treatment. These include: canal preparation and debridement; canal obliteration; and the reaction of infected periapical tissues to each method of treatment. Accepted in vitro procedures will be utilized to compare canal preparation and obliteration. Clinical treatment of pulpally and periapically infected monkey teeth, using a standardized infecting procedure, will be evaluated histopathologically on the basis of periapical tissue vitality and repair; arrangement of the periodontal ligament at the apical foramen and the presence of residual bacteria. Results of these studies will give more accurate means for evaluating each treatment method.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

2.0269, DEVELOPMENT AND EVALUATION OF IMPROVED DENTAL RADIOGRAPHIC SYSTEMS WITH EMPHASIS ON FACTORS INFLUENCING DIAGNOSTIC PERFORMANCE

R.L. Webber, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Diagnostic Methodology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00065-08 CI)

For summary: see 1.0187.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $35,479

2.0270, ENHANCEMENT OF DIAGNOSTIC IMAGES

R.L. Webber, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Diagnostic Methodology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00211-03 CI)

For summary: see 1.0188.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $29,748

II. PERIODONTAL DISEASE

2.0271, EVALUATION OF SURGERY AND ANTIBACTERIAL AGENTS IN CONTROL OF PERIODONTITIS

W.E. Wright, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Clinical Dental Services Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00239-02 IR)

The effectiveness of conventional mechanical hygiene alone and in combination with topical applications of sodium bicarbonate-sodium 'paste' to control accumulations of oral bacteria will be compared in subjects with moderate periodontitis. Each subject will also undergo periodontal pocket reduction surgery in two of four posterior quadrants to allow assessment of this commonly used mode of periodontal disease therapy. Evaluation criteria will be (1) motile microscopic forms and white blood cells obtained from periodontal pockets will be viewed and numerically estimated by phase microscopy, (2) gingival sulci bleeding index and (3) measurements of gingival attachments relative to the cemento-enamel junction and gingival margin.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$18,666

2.0272, THE DETECTION OF OCCULT INFECTIOUS DENTAL LESIONS BY BONE IMAGING

T.M. Sullivan, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *1400 Vet. of Foreign Wars Pkwy, West Roxbury, Massachusetts* 02132 (690-001-F)

The objective of this project was to evaluate the clinical usefulness of bone imaging for the detection of common dental diseases.

Patients scheduled for diagnostic bone scans were asked to consent to additional imaging of the head. Within one week of imaging, each patient was examined by staff members of the Dental Service for dental disease. The findings from both services were then compared for each patient.

Twenty-five patients consented to participate. Three head images were made with a scintillation cmaera. Dental examinations included intraoral radiographs, clinical evaluations of hard and soft tissues, and a dental history. Each patient's mouth was divided into 4 upper and 4 lower quadrants, and each quadrant was scored for the positive findings from both types of examinations.

Fourteen of 25 subjects had at least one positive image area within the jaws. Positive image areas were observed for 11 of 11 quadrants with healing bone lesions, 20 of 22 with acute disease, 19 of 55 with chronic, subacute disease, and 6 of 102 quadrants considered disease-free by dental criteria. It was concluded that jaw imaging may be useful in detecting incipient disease or the reactivation of quiescent disease, before it is apparent by routine dental diagnostic procedures.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0273, THE CHANGES IN OSSEOUS AND GINGIVAL TISSUES FOLLOWING THE INTERDENTAL DENUDATION PROCEDURES - A SIX MONTH STUDY

G. Kazandjian, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *800 Poly Pl., Brooklyn, New York* 11209 (527-001-P)

In order to assess whether there is bone loss or bone regeneration following performance of the Interdental Denudation Procedure (IDP) on teeth suffering from moderate or severe periodontal disease with bony defects, the following experimental study is designed.

Sufficient number of patients to provide 50 experimental sites and 50 control sites will be selected for periodontal treatment. Patients will be screened according to criteria designed for Patient Selection and Experimental Site Selection. The operative procedure for the test (IDP) and control (primary closure) experimental sites will be similar in all aspects except for the tested variable: soft tissue closure of the interdental area. For the test sites the flap closure will not cover the interdental bone and for the control sites the flap ends will be brought to cover the interdental bone for primary healing. Prior to, and during the surgical procedure, pertinent measurements, photographs and radiographs relative to the height of the interdental bone wil be taken. Linear measurements will be made from a fixed point (stent.) All patient and experimental sites will be followed for six months, during which time these sites will be observed and monitored. At the end of six months all those sites will be re-entered surgically by means of an open curettage performed on buccal aspect only. During the re-entry, all pertinent measurements, photographs and radiographs will be taken again. The initial measurements will then be compared with the re-entry measurement and conclusions drawn.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0274, LOCAL DEGERMING TO REDUCE BACTEREMIA DURING DENTAL SCALING

T. Witzenberger, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *1481 W. 10th St., Indianapolis, Indiana* 46202 (583-001-I)

Twenty patients with chronic periodontal disease, requiring subgingival scaling as a part of their periodontal therapy, will be selected. Each patient will receive a comprehensive periodontal examination including radiographs, pocket chartings, and various indices to evaluate gingival health and oral hygiene status. Two similarly involved areas in each subject will be selected, one to serve as a control and the other as the experimental site. All subjects will have 5cc venous blood samples drawn at specified time intervals before, during, and after subgingival scaling. Blood samples will be cultured anaerobically and positive cultures subcultured to identify individual colonies of micro-organisms. The control group will receive subgingival scaling in the usual manner; the experimental group will also receive three minute irrigation of the soft tissue pockets with a providone-iodine solution (Betadine) prior to scaling. The incidence of bacteremia observed in the control group will be correlated with that seen in the experimental group to determine if the irrigation techniques is effective. In addition, the incidence of bacterima will be correlated with such factors as pocket depth, the various indices recorded, and the irrigation technique itself.

SUPPORTED BY

U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

2.0275, LONG TERM TETRACYCLINE STUDY

I.W. Scopp, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *1st Ave. at E. 24th St., New York, New York* 10010 (630-001-F)

Tetracycline hydrochloride is administered by some periodontists in small doses over long periods of time as adjuvant to conventional therapy. There are no studies on humans to determine the effectiveness of this regimen. It is the purpose of this study to determine whether the use of low doses of tetracycline over long periods of time as adjunctive to conventional therapy is an advantage. The study is a double blind crossover project on patients treated in a hospital dental service with random selection of patients receiving either tetracycline or placebo capsules. The study of the effects of tetracycline therapy on 15 patients over a three month period revealed that there were no significant differences between the placebo group and tetracycline treated groups in relation to (1) Gingival Index, (2) Debris Index and (3) Papillary Bleeding. A marked improvement (PL 0.002, PL 0.05) in the Gingival Index occurred after 3 months of treatment in each group. Papillary bleeding was significantly reduced after 3 months of treatment in the tetracycline group, and similar but non-significant trends were also observed in the placebo group. The Debris Index in both experimental and placebo groups showed no significant change after treatment for three months. The data suggests that tetracycline therapy does not appreciably alter either the Gingival Index, Debris Index, or the Pillary Bleeding Index, over a 3 month period, as the values fell within the range reported for the placebo controls. A paper summarizing the study is being prepared for publication.

SUPPORTED BY

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Medicine & Surgery funds n.a.

2.0276, INVESTIGATION OF CARDIAC ARRHYTHMIAS DURING PERIODONTAL SURGERY

R.E. Davenport, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *5000 W. National Ave., Wood, Wisconsin* 53193 (695-001-F)

In this project 20 patients (average age 45 years) who were scheduled for periodontal surgery were examined by a cardiologist and deemed to be free of cardiovascular disease. The examination included an electrocardiogram and chest x-ray. For patients over 50 years of age a stress test was also included. Patients in the study were examined for the presence of cardiac arrhythmias during a control period and during periodontal surgery utilizing a Holter monitor portable electrocardiogram. Mucoperiosteal flap surgery was performed utilizing 2% xylocaine with eprinephrine 1:100,000. The objective of the project was to determine if periodontal surgery under local anesthesia was associated with an increase in the number cardiac arrhythmias over those seen during a period of normal activity. Particular attention was given to whether the dose of local anesthetic with epinephrine or the length of the procedure was associated with an increase in the number of cardiac arrhythmias.

Results of this project have shown that periodontal surgery was not associated with a significant change in the number of arrhythmias over those seen during a period of normal activity. In addition, no significant correlation between either the length of the procedure or the dose of local anesthetic and the number of arrhythmias was found. The mean dose was 9.62cc and the mean time was 114 min. Of particular interest was the absence of a systemic effect of epinephrine. Average maximal heart rates were faster (114.9) during the control period than during periodontal surgery (100.3).

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

2.0277, PREVENTIVE DENTISTRY FOR THE VA PATIENT

D.E. Patthoff, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Martinsburg, West Virginia* 25401 (613-001-I)

This nine-month feasibility study attempts to establish the potential of the intraoral photograph and the ChromascanTR as a diagnostic tool for dentists and as an accurate objective and personalized feedback mechanism for patients. It is conducted in three sequential phases.

Phase I establishes the reliability of the ChromascanTR readings of simulated normal and diseased gingival colors. Concurrent validity of the ChromascanTR as a measure of color is established through correlation of readings with the Munsell color system. In addition, the ChromascanTR readings of photographs of gingival colors reflected in eight reddish Munsell color tabs will be correlated with ChromascanTR readings of the actual Munsell color tabs.

In Phase II, the ability of random VA dentists to detect reversible gingival pathology through photographs is assessed. Photographs depicting six reversible periodontal conditions, i.e., formation of plaque, gingival color change, gingival texture change, gingival form change, and gingival bleeding; are obtained from dental patients at two time periods. Using these photographs, 20 dentists are asked to make judgements about the absence or presence of periodontal conditions and the changes in these conditions when photographs from time I and time II are compared. The judgements made by the dentists are correlated with those made by calibrated dentists during a clinical examination.

In Phase III, the ability of patients to recognize clinical conditions manifested by reversibe periodontal diseases are assessed. Specifically, 25 patients are given a brief, highly structural program, and are asked to make the same judgements as the 20 dentists in Phase II. These judgements are correlated with those made by the calibrated dentists during the clinical examination.

The findings from this feasibility study will be incorporated into the design of a research project to test the effectiveness of the photographic and spectrophotometric method as a patient eduation tool and as a diagnostic tool in a highly structural and personalized preventive dentistry program at the Martinsburg VA.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

2.0278, HUMAN MOUTH AIR VOLATILES IN PERIODONTAL DISEASE

P. Zelson, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *38th & Woodland Aves., Philadelphia, Pennsylvania* 19104 (642-003-I)

The proposed study is a collaborative study between the Veterans Administration Hospital and the Monell Chemical Senses Center at the University of Pennsylvania. Its principal purpose is to define the type and abundance of small organic volatiles in the mouth air and saliva of subjects whose oral cavities range from healthy to severe periodontal involvement.

Previous studies have demonstrated that levels of specific metabolites in human mouth air and certain body fluids are excellent indicators of metabolic and pathologic processes. Changes in the presence and/or concentration of small organic volatiles found in the mouth air and above incubated saliva of humans may aid in the early diagnosis of degenerative oral tissue diseases, such as periodontal disease, as well as systemic disorders which manifest themselves in the oral cavity. There is also evidence that specific oral metabolites may contribute to the etiology and/or pathogenesis of periodontal disease.

The level of oral pathology will be rated by four common oral health indices: the gingival, plaque, periodontal and periodontal disease indices. Organic molecules in mouth air and saliva will be evaluated by gas chromatography and gas chromatography-mass spectrometry. These procedures will allow a large number of metabolites to be simultaneously monitored at the parts per million, to parts per billion level. The amounts of volatiles in both mouth air and above incubated saliva will be correlated with the oral health indices noted above by the appropriate statistical methods.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

2.0279, TASTE, PERIODONTAL DISEASE AND NUTRITION

P.R. Zelson, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *38th & Woodland Aves., Philadelphia, Pennsylvania* 19104 (642-004-I)

This study will help clarify the relationship of taste sensitivity and a subject's nutritional status to the etiology and/or pathogenesis of degenerative periodontal changes. This will allow for early detection and prevention of periodontal disease via changes in salivary or serum minerals as measured by atomic absorption spectroscopy.

Specific oral metabolites may contribute to the etiology of oral tissue diseases. One study shows that the presence of larger than normal amounts of copper, in serum, is positively correlated with an increased incidence of periodontal disease. Thus a rationale exists for examining the mineral content of serum and saliva. Also, it is important to know whether taste sensitivity is altered in these subjects since this may contribute to an abnormal nutritional status.

Oral pathology will be rated by four common indices: gingival, plaque, periodontal and periodontal disease. A dietary questionnaire and a 24 hour dietary recall will be obtained. Taste sensitivity will be determined for the following solutions: sucrose, citric acid, sodium chloride and quinine sulfate. Pure saliva will be collected by placing sterile plastic Lashley cups over Stenson's duct. The fluid will be collected for a period of fifteen minutes and stored at 4 degrees C for mineral analysis. In addition, 8 cc of venous blood (for serum) will be collected.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

2.0280, THE EFFECT OF CITRIC ACID ON CORONALLY REPOSITIONED FLAPS

T.N. Sims, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-007-I)

The purpose of this study is to evaluate the effect of citric acid on attachment of coronally repositioned flaps to root surfaces. Patients with areas of bilateral recession and adequate attached gingiva will receive coronally repositioned flaps. The control tooth will receive a citric acid treatment as described by Registar and Burdick prior to coronal repositioning. This is based on experimental evidence that dentin or cementum demineralization accelerates reattachment. Pre-and post- operative evaluation will include stent measurements of recession, pocket depth, attached gingiva, and boney dehiscence. Soft tissue evaluation via the Gingival Index will also be performed. Evaluation will occur at 1 and 2 weeks, and 1,3, and 6 months postoperatively. It is the intention, therefore, of this study to evaluate a new modality of treating root recession in order to aid in prevention of caries, trauma (abrasion), and sensitivity, as well as improvement of esthetic appearance.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

2.0281, EFFECTS OF SALICYLATE INGESTION ON THE HEALTH OF TOOTH SUPPORTING ALVEOLAR BONE

J.E. House, U.S. Veterans Admin., Dept. of Medicine & Surgery, Outpatient Clinic, Dental Service, *17 Court St., Boston, Massachusetts* 02108 (750-001-P)

The purpose of this study was to determine if the ingestion of large amounts of salicylates on a daily basis for long periods of time has any effect on the health of the dentition. Specifically, we wished to know if salicylates can inhibit inflammatory responses in bone associated with periodontitis, a chronic destructive disease of tooth-supporting alveolar bone. To test the hypothesis, a comparison was designed between two groups of subjects in terms of the amount of bone support surrounding their teeth as measured on intraoral radiographs.

Ninety-eight volunteers with verified histories of daily salicylate ingestion at high doses (10 to 20 tablets per day) for extended time periods were selected from among patients of the Arthritis Clinic. A second group, consisting of an equal number of non-users of salicylates, were selected from the Longitudinal Oral Health Study, an ongoing study in this Dental Service. The two groups were matched with respect to age and the types of removable prostheses worn. The subjects ranged in age from 32 to 87 years.

To date, radiographic measurements, for all subjects, have been completed and data statistically analyzed. It appears there is a statistically significant prevention of alveolar bone loss among the salicylate using group compared to the control group. Presently, the results are being written for publication.

SUPPORTED BY
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Medicine & Surgery funds n.a.

2.0282, COMBINED DENTAL RESEARCH PROGRAM - PERIODONTICS SECTION - ENDODONTIC SECTION

W.C. Bird, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Periodontics Section, *1201 Broad Rock Rd., Richmond, Virginia* 23249 (652-001-P)

Longitudinal Evaluation of Free Autogenous Gingival Grafts: 91 patients with biolateral areas of insufficient attached gingiva have been evaluated from 6 mos. to 3 yrs. 102 free gingival grafts were placed with the contralateral area serving as control. Base line readings were statitically similar on both sides. To date, data show no significant differences on the control side except for a decrease in plaque & gingival indices. The experimental side shows an increase in keratinized and attached gingiva, a significant decrease in plaque & gingival indices and no changes in sulcus depth, recession or attachment loss. Since no significant attachment loss changes were evident on either control or experimental sides, even with an initial 0.35mm. of attached gingiva, it seems that control of plaque and inflammation is sufficient to prevent recession & loss of attachment in spite of inadequate dimensions of attached gingiva. Further longitudinal documentation is necessary.

The purpose of this project was to study the effect of a filling material containing lead & paraformaldehyde (N2) upon (1) the lead content of the blood and vital organs (liver, kidney, spleen, brain) (2) The peraipical tissues. Root canals in bicuspid teeth of 50 dogs were filled with N2 paste over a 2 yr. period. 43 dogs have been sacrificed to date and the remaining 7 will be sacrificed by Nov. 3, 1978. Preliminary analyses of lead levels in the blood & vital organs revealed no significant increase with time. Decalcification of teeth and jaws from the sacrificed animals is in progress & the histopathologic results should be available in the second and third quarters of this fiscal year.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

PREVENTION - PLAQUE

2.0283, EDENTULOUSNESS (NO TEETH) AND BLACK HAIRY TONGUE

B.C. Rover, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Perry Point, Maryland* 21902 (641-001-I)

Edentulousness and Black Hairy Tongue is not rare among the veteran population at Perry Point VAMC. In patients with missing or no teeth almost 33% have some form of coated tongue. According to this clinical observation, edentulous patients (those without teeth) appear to have various forms of the disease more frenquently than those with teeth (dentulous). The role of tooth loss has played no part in earlier research of Black Hairy Tongue. In geriatric population particularly, and also in many physically ill populations, the loss of teeth is a clearly significant event of the oral cavity. This study proposes to examine the degree of association between edentulousness and Black Hairy Tongue to further the understanding of the etiology of this disease. preliminary study was conducted to determine if there was any substance to the clinical observations mentioned above. Fifty patients were chosen at random evenly divided between dentulous and edentuluousness and Black Hairy Tounge. Data were collected on 18 variables. From the results, it was established that a strong relationship existed between edentulousness and Black Hairy Tongue, that also there seemed to be almost no relationship between cigarette smoking habits and HBT, and there appeared slight relationship between BHT and age. This study proposes a cross-sectional design with simple random sampling of subjects and two data collection phases - first data collection to include clinical data items and second, data collection from medical records and dental records. Implications from this study include the role of edentulouness in the etiology of Black Hairy Tongue, the utility of biocenologic approach to research in an area where there is an abundance of natural flora in a healthy ecologic community, the mouth with further treatment implications such as improved oral hygiene.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0284, THE ROLE OF PLASMIDS IN THE PATHOGENESIS, ECOLOGY AND TAXONOMY OF THE ORAL MICROFLORA

D.J. LeBlanc, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Microbiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00174-04 LMI)

For summary: see 1.0130.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$12,213

2.0285, MECHANISMS OF SECRETORY ANTIBODY INDUCTION

P.C. Montgomery, University of Pennsylvania, School of Dental Medicine, Dept. of Microbiology, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (P50 DE 02623-120013)

The secretory immune system is characterized by the localized production of antibodies in glandular areas or at mucosal surfaces. Secretory antibodies appear to play specific roles in enhanced resistance to a variety of infectious agents. The proposed investigations are designed to study mechanisms involved in secretory antibody induction in order to assess the interrelationships between local and systemic immunity. Animal models will be used to assess questions concerning the interdependence of localized immune responses and existence of cell homing mechanisms. In addition, the role of the liver in the secretory immune system will be investigated. Studies on the cellular aspects of secretory antibody induction will include the development of methods to determine the capacity of cells derived from solid secretory organs to participate in antibody responses and the role of the T cell in the secretory IgA antibody response. The immuneresponsiveness of the salivary gland will be investigated. Data on the patterns of immune responses will be coupled with studies of underlying cellular events in order to provide insight into the manner by which antigens elicit secretory antibodies as well as how the required molecular information is made available to the antibody generating secretory sites.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$148,643

2.0286, MOLECULAR MEDIATORS OF ORAL DISEASE

D.A. Chambers, University of Michigan, Ann Arbor Campus, Medical School, Dept. of Dermatology, *1335 E. Catherine St., Ann Arbor, Michigan* 48104 (R01 DE 04373-03)

The objective of this project is to examine the role of cellular immunity in periodontal disease. In particular, the molecular events related to plaque-mediated lymphocyte activation and its control by regulatory molecules, e.g. cyclic nucleotides, prostaglandins, lymphokines, serum activators or inhibitors will be studied in specifically designed cell-culture systems derived from mice and humans. Molecules of specific interest (lymphokines, etc.) will be purified and studied in an effort to define their mechanism of action. Particular emphasis will be placed on a study of the lymphokine, osteoclast activating factor (OAF), in the pathophysiology of periodontal disease as well as other bone diseases. Additionally, the role of 'growth proliferative' cyclic GMP dependent enzymes will be investigated in both normal and aberrant cellular proliferative processes, e.g., neoplasia and leukoplakia. From the knowledge gained in these studies, specific therapies for oral disease will be designed.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

PREVENTION - CALCULUS REMOVAL & MINERALIZATION INTERFERENCE

2.0287, SEM STUDY OF INSTRUMENTED LONGITUDINALLY SPLIT TOOTH ROOTS

T.N. Sims, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-003-P)

A total of 8 teeth, 16 samples, have been fixed, critical pointed dryed, plated and observed at 50 to 5000 magnification under scanning electron microscopy at the U. S. C. School of Engineering. Preliminary observations suggest the effect of the curet and the ultrasonic scaler is variable dependent on the nature of the root and the amount of deposits. The curet leaves sheered mounts of tightly adherent calculus and cemention exposed. The cavitions leave a rougher surface that appears to be freer of calculus, even in root depressions. On a clean root surface, the curet and the ultrasonic instrument leave rough surfaces. This appears to occur whenever cemention is removed. The curet left a furrowed appearance corresponding to the contours of the instrument. The ultrasonic instrument leaves a clean indistinct uniform 'pebbly' surface. Finding good specimens has been difficult and specimens can be easily ruined due to the delicate nature of the splitting technique.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

2.0288, DENTAL CALCULUS - MORPHOLOGICAL ANALYSIS THROUGH OPTICAL MICROSCOPY

H. Gendelman, Universidad Nacional de Cordoba, Facultad de Odontologia, Dept. of Pathological Anatomy, *5000 Cordoba, Argentina*

The study of dental calculus through optical microscopy with incidental light in a variable angle, has permitted us to observe three-dimensionally: the superficial morphology, the internal structure and the fractugraphy of these solids of biological origin.

The obtained documentation made possible to register: calcification nucleus, microcavities, stratum, fractugraphies and poliedric structures at calculus-tooth interface level.

SUPPORTED BY

Universidad Nacional de Cordoba $6,000

PREVENTION - INFLAMMATION

2.0289, STUDIES ON LEUKOCYTE CHEMOTAXIS

E. Schiffmann, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00006-19 DB)

The ultimate goal of this project is to understand the molecular events as cells migrate along a chemical gradient. Most of our studies utilize leukocytes and small formylmethionyl peptide attractants. Tyrosine appears to be an essential component of the cell surface receptor, and certain hydrophobic peptide esters inhibit agonist-receptor interaction. The events triggered by the interaction of peptide with a surface receptor include activation of both a membrane phospholipase and a protein methylesterase; these may contribute to chemotaxis by increasing membrane fluidity and inducing conformational changes in contractile proteins respectively. The cell may terminate its response to formylmethionyl peptides by oxidizing the methionyl sulfur of the attractant. Other regulatory systems under study include the antichemotactic effects of materials derived from tumors as well as glucocorticoids. Initial studies on fibroblast chemotaxis indicate that motility in this cell may involve processes similar to those in the leukocyte.

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Research $203,139

PREVENTION - CONNECTIVE TISSUE METABOLISM

2.0290, PHENYTOIN GINGIVAL HYPERPLASIA IN THE FERRET

C. Siew, American Dental Assn., *211 E. Chicago Ave., Chicago, Illinois* 60611 (N01RR82147 (CONTRACT))

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health, Div. of
Research Resources funds n.a.

2.0291, ACID PHOSPHATASES IN DEVELOPING BONES AND TEETH

S.U. Toverud, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Pharmacology/Oral Diagnosis, *Chapel Hill, North Carolina* 27514 (R01 DE 05210-01)

The overall objective of the proposed project is to separate, characterize and localize the acid phosphatases in developing bones and the enamel organ of tooth buds and to determine the effect of parathyroid hormone and vitamin D in vivo/in vitro on the different phosphatases, in order to gain insight into the role of these enzymes in hard tissue formation and function.

After solubilization of the acid phosphatases in rat tissue homogenates, separation and purification of the enzymes will be achieved by means of ion-exchange chromatography and polyacrylamide disc gel electrophoresis. The enzymes will be characterized in terms of molecular size, pH optimum, thermolability, kinetic characteristics for various substrates and the influence of various effectors on the kinetic characteristics.

Information concerning the function of the various acid phosphatases will be obtained by determining (a) the specificity of the enzymes for potential in vivo substrates; (b) localizaton of enzymes in cells and cellular organelles and (c) by determining the effect of vitamin D and parathyroid hormone on activity and tissue level of specific acid phosphatases in bone and tooth buds in vivo and in bone cultured in vitro. The latter studies will be carried out with vitamin D-deficient suckling rats, or, for the in vitro experiments, with bones from such rats. Localization of the enzymes will be determined by means of (a) biochemical studies on dissected tissues containing primarily one type of cell; (b) cytochemical techniques at the light and electron microscopic levels using specific substrates and inhibitors determined biochemically; and (c) immunocytochemical techniques using antiserum to one or more specific phosphatase.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $34,310

2.0292, CYTODIFFERENTIATION OF PERIODONTAL LIGAMENT FIBROBLASTS

J.A. Yee, Texas Tech University, School of Medicine, Dept. of Anatomy, *P.O. Box 4340, Lubbock, Texas* 79409 (R23 DE 04371-03)

On the basis of their morphology the cells of the periodontal ligament (PDL) appear to comprise a homogenous population. However, their response to various types of stimuli suggests that the population consists of fibroblasts and their precursors as well as the progenitors of osteoblasts, cementoblasts and possibly osteoclasts. Since it is not possible to distinguish these progenitor subpopulations morphologically little is known about their nature or their relationship to the functional fibroblasts. It is the major goal of the proposed project to characterize the nature of the response of PDL fibroblasts to specific stimuli wth the aim of understanding their functional and differentiative capacity.

Two basic forms of stimulation are being applied to the periodontium. The first, orthodontic tooth movement, is being used to study the osteogenic response of PDL fibroblasts. By examining certain regions along the alveolar bone surface as well as areas in the central portion of the PDL it is possible to examine the nature of both the osteogenic reponse as well as a fibrogenic response. The latter is involved in repair of damage inflicted on the PDL by tooth movement. The second system being employed in these studies is one which involves a bone resorptive response. In this model parathyroid hormone administartion is being used to stimulate alveolar bone resorption. The nature of the response of PDL fibroblasts during the resorptive response is being assessed to determine if the osteoclasts generated arise from local progenitors or if they are derived from a blood-borne precursor.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

III. SOFT TISSUE DISEASES

HERPES SIMPLEX VIRUS INFECTIONS - EPIDEMIOLOGY

3.0001, NATURAL HISTORY OF ORAL LESIONS ENCOUNTERED IN THE SOLDIER

J.C. Adrian, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Pathology, *Washington, District of Columbia* 20012 (DA0H6030)

To recognize, characterize and develop effective therapeutic measures for those lesions and conditions which effect the soldier due to military duty. The recognition of environmental and other factors which participate in the etiology of lesions and conditions unique to the military or are casually related to military duty will enable the development of interceptive or therapeutic measures.

To detect through clinical and/or microscopic observation oral lesions or conditions unique to the military population. To identify oral lesions or conditions which, though not unique to the soldier, are etiologically related to he performance of duty. Once identified the natural history including etiology, therapy, and prognosis will be established utilizing appropriate methods such as surveys, animals, and human investigations.

SUPPORTED BY
U.S. Dept. of Defense, Army,
Medical Research &
Development Command, Inst.
of Dental Research funds n.a.

HERPES SIMPLEX VIRUS INFECTIONS - ETIOLOGY

3.0002, RECURRENT HERPES VIRUS HOMINIS INFECTION

J.C. Overall, Utah Higher Education System, University of Utah, School of Medicine, *1400 E. 2nd S., Salt Lake City, Utah* 84112 (N01AI52532 (CONTRACT))

The pathogenesis of facial mucocutaneous Herpesvirus hominis (HVH) infections will be studied in 20 volunteers by correlating symptoms, histopathology, and HVH titers in lesions and saliva. All HVH isolates will be typed and tested for sensitivity to adenine arabinoside monophosphate (Ara-A-MP) and to disodium phosphonoacetate (PAA). In Phase II, 75 otherwise healthy subjects with facial HVH infection and 21 immunosuppressed patients with facial HVH infection will be randomly assigned to topical treatment with either 3% Ara-A-MP, 5% PAA, or placebo ointment in a prospective, double-blind clinical trial.

III. SOFT TISSUE DISEASES

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$46,025

3.0003, SJOGREN'S SYNDROME, APHTHOUS ULCERS & BEHCET'S SYNDROME

D.P. Martin, Litton Bionetics Inc., *5516 Nicholson Ln., Kensington, Maryland* 20795 (N01DE72405 (CONTRACT))

Litton Bionetics will provide testing for antinuclear antibody by fluorescent antibody and radioimmunodiffusion assays ten rhesus monkeys of less than one year of age. Ten animals negative to both tests for antibody will be chosen, all of which are negative to a tuberculin skin test using Old Tuberculin. These animals will be inoculated intracerebrally, intraperitoneally, intravenously, and subcutaneously as directed by the Project Officer with preparations of appropriate biopsy specimens supplied by NIDR. These animals will be maintained for two years and observed daily for early signs of clinical disease. If an animal should develop any disease, NIDR will be notified immedately. copy of the clinical records of each animal for each four-month period will be supplied to NIDR.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$32,821

3.0004, BIOCHEMICAL STUDIES ON THE MAJOR STRUCTURAL PROTEINS OF HERPES SIMPLEX VIRUS

G.H. Cohen, University of Pennsylvania, School of Dental Medicine, Dept. of Microbiology, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (P50 DE 02623-120002)

Experiments now in progress are designed to analyze the synthesis, processing and structural properties of herpes simplex virus type 1, (HSV-1) envelope glycoproteins (gp). Antisera to the undenatured type common glycoprotein (gp59 or D) is used as an immunologic probe in pulse-chase experiments to focus specifically on the synthesis of gp59. These experiments show that a smaller glycoprotein, gp52, is a precursor of gp59. Tryptic peptide analysis shows that gp52 and gp59 share methionine peptides. Furthermore, none of the methionine residues of gp59 are shared with the larger molecular weight glycoproteins of HSV-1. Processing from gp52 to gp59 does not require protein synthesis but does involve several glycosylation steps. Evidence from these studies favor a mechanism as follows: a 50K core polypeptide is synthesized starting at 2 hr post infection and is glycosylated within 2 minutes by addition of an oligomannosyl core moiety. The precursor glycoprotein (gp52) is processed by further glycosylation to a more acidic and heterogeneous molecule with a molecular weight of 59,000. Experiments are planned to analyze further details of this processing, to determine the contribution of the protein and carbohydrate moieties induction of neutralizing antibody and to assess the role of this glycoprotein in the infectious process.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$155,724

3.0005, HERPES SIMPLEX VIRUS - LATENCY

H.O. Openshaw, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Laboratory of Oral Medicine, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00123-06 LOM)

The object of this project is to study the pathogenesis of latent herpes simplex virus infection in both peripheral ganglia and in brain. Biological studies are designed to elucidate factors that induce virus reactivation. Molecular studies are concerned with the state of the latent viral genome, the extent of viral expression, and the mechanism by which latency is established and maintained.

BIBLIOGRAPHIC REFERENCES: Openshaw, H., Ashen, L.V.S., Wohlenberg, C.R., Sekizawa, T., and Notkins, A.L.: Acute and latent infection of sensory ganglia with herpes simplex virus: Immune control and viral reactivation. J. Gen. Virol. 44:205-215, 1979. Wohlenberg, C., Openshaw, H., and Notkins, A.L.: In vitro system for studying the efficacy of anti-viral agents in preventing the reactivation of latent herpes simplex virus. Antimicrobial Agents and Chemotherapy 15:625-627, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$367,291

3.0006, HERPES SIMPLEX VIRUS - CELL-MEDIATED IMMUNE MECHANISMS AND INTERFERON

J.J. Hooks, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Laboratory of Oral Medicine, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00219-03 LOM)

The objective of this research project is to determine the role of viruses and interferon in immunologic and immunopathologic processes.

The observation that immune interferon could be produced by peripheral blood leukocytes in vitro on an immune specific basis suggested that it might be produced in vivo in various autoimmune disorders. We found immune interferon in the sera of patients with active immunologic diseases, such as systemic lupus erythematosus, rheumatoid arthritis, scleroderma and Sjorgren's syndrome. Furthermore, the presence of interferon was correlated with clinical disease activity.

It is possible that the production of interferon may contribute to immunologic aberrations in autoimmune diseases and also protect the already compromised host from viral infections.

BIBLIOGRAPHIC REFERENCES: Hernandez-Asensio, M., J.J. Hooks, S. Ida, R.P. Siraganian, and A.L. Notkins. Interferon-induced enhancement of IgE-mediated histamine release from human basophils requires RNA synthesis. J. Immunol. 122:1601-1603, 1979. Hooks, J.J., H.M. Moutsopoulos, S.A. Geis, N.I. Stahl, J.L. Decker, and A.L. Notkins. Immune interferon in the circulation of patients with autoimmune diseases. N. Engl. J. Med. 301:5-8, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$214,701

3.0007, RECEPTORS, MEMBRANES AND DISEASES

P.R. McClintock, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Laboratory of Oral Medicine, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00255-01 LOM)

Cell surface receptors for viruses and polypeptide hormones were studied in cells of murine and human origin. The human membrane receptors for Encephalomyocarditis virus were found to be quantitatively and qualitatively different from those on murine cell membranes, although cells of both species are susceptible. Another class of membrane receptors, those for the polypeptide hormone insulin, was studied following infection with Herpes Simplex and other viruses. The number of insulin recptors decreased following herpes simplex and vesicular stomatitis viruses but not after infection with measles and Sinbis viruses.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$145,020

HERPES SIMPLEX VIRUS INFECTIONS - PATHOLOGY

3.0008, HERPES REACTIVATIONS AFTER CRANIAL NERVE SURGERY

J.A. Armstrong, University of Pittsburgh, Graduate School of Public Health, Dept. of Microbiology, *4200 5th Ave., Pittsburgh, Pennsylvania* 15260 (R01 AI 15299-02)

After microvascular decompression of the trigeminal nerve for relief of tic douloureux, about 70% of patients with a positive history of cold sores develop herpes lesions with onsets 2-5 days after surgery. We will administer interferon for five days, commencing the day prior to surgery, to 20 patients per year in order to modify the disease or reduce its frequency. Interferon in serum and throat washes will be assayed. A control group will receive a placebo. The patients, and others including those undergoing VIIth nerve surgery for hemi -facial spasm will be followed clinically, virologically and immunologically. The purpose of this phase of the study is to examine events occurring between the time of stimulus (surgery) and the appearance of overt lesions. This early phase of the pathogenesis of recurrent herpes is not usually available to investigators. We will ascertain the time of appearance of herpes virus in the oropharynx, (we commonly find the virus in throat washes), look, by fluourescent antibody methods, for the appearance and location of cells containing viral antigen in this site and follow humoral and cell mediated immunity to herpes virus.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Allergy & Infectious Diseases	$55,800

3.0009, THE INFLAMMATORY RESPONSE IN VIRAL INFECTION

C.A. Daniels, Duke University, School of Medicine, Dept. of Pathology, *Box 3711, Durham, North Carolina* 27710 (R01 DE 04609-02)

In man and experimental animals the evidence strongly indicates that inflammation plays a significant role in the resistance to and in the recovery from viral infections. Once a virus gains entry, the host's polymorphonuclear leukocytes (PML), macrophages, and lymphocytes respond, attempting to eradicate the invading pathogen and to prevent the spread of the virus. The role various types of inflammatory cells play in vivo is presently unclear. Leukocytes may facilitate recovery by phagocytosing and killing virus particles, lysing infected cells, and preventing the spread of virus from cell-to-contiguous cell. Each of these functions can be examined in tissue culture. Using these techniques we propose to define the role of various types of inflammatory cells in an effort to understand the cellular response to in vivo infections. We hypothesize that the reason man and certain strains of mice have recurrent and sometimes lethal viral infections is because their leukocytes are incapable of containing them.

Herpes simplex virus (HSV) is the virus we intend to study because it spreads by each of the routes by which viruses are known to spread (i.e., extracellularly, from cell to contiguous cell, and to daughter cells in mitosis). PML, macrophages, and lymphocytes will be isolated from three separate patient populations: 1) Those who have never had herpetic infections, 2) individuals with infrequent disease and 3) subjects with multiple, frequent recurrent infections. In addition the leukocytes from HSV-resistant and susceptible inbred mouse strains will be assessed for the antiviral activity of their leukocytes. In quantitative assay systems we shall determine how effective the various human and murine leukocytes are in containing virus infections in vitro. Having assayed the antiviral activity of the various types of leukocytes we shall be able to detect which leukocytes are dysfunctional and to what extent they are incapable of containing the infection. Our ultimate goal is to develop in vitro tests for detecting susceptible states in man and to develop a basis by which we might therapeutically reverse the susceptibility of the patient and thereby protect him from infection.

BIBLIOGRAPHIC REFERENCES: Pozner, L.H., Daniels, C.A., Croker, B.P., Cohen, H.J. and Logue, G.L., Replication of Type I Herpes Simplex Virus in Primary Cultures of Hairy Cell Leukemic Leukocytes. American Journal of Pathology 90:187, 1978. Daniels, C.A., Kleinerman, E.S., Snyderman, R., Abortive and Productive Infections of Human Mononuclear Phagocytes by Type I Herpes Simplex Virus. American Journal of Pathology 91:119, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$46,574

3.0010, SIGNAL REQUIREMENTS FOR LYMPHOCYTE ACTIVATION

D.L. Rosenstreich, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Cellular Immunology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00261-01 LMI)

T lymphocytes require macrophage help in order to proliferate in vivo in response to mitogens and antigens. The compound phorbol myristate acetate (PMA) will replace macrophages and enable T cells to proliferate in response to a mitogenic but not an antigenic stimulus. cells primed with PMA will also proliferate in response to a soluble product derived from the culture of antigen pulsed macrophages. We are currently examining the product in the culture supernatant of antigen pulsed macrophages to see if it exhibits the theoretically predicted properties of 'processed antigen'--i.e., antigen specificity and genetic restriction in its effect or if it is a non specific T-cell triggering molecule.

BIBLIOGRAPHIC REFERENCES: Rosenstreich, D. L. and S. M. Mizel. The participation of macrophages and macrophage cell lines in the activation of T-lymphocytes by mitogens. Immunological Reviews 40: 102-135, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$38,769

HERPES SIMPLEX VIRUS INFECTIONS - DIAGNOSIS & TREATMENT

3.0011, NEW ANTIVIRAL NUCLEOSIDES FOR OCULAR AND OTHER HERPES

D.M. Albert, Harvard University, Boston Campus, Massachusetts Eye & Ear Infirmary, Howe Laboratory, *243 Charles St., Boston, Massachusetts* 02114 (R01 EY 02268-02)

The proposed studies involve the in vivo investigation of a new class of antiviral thymidine analogs, developed in the same laboratory where IdUrd was conceived and synthesized. The therapeutic efficacy of one of these compounds, 5-iodo-5'-amino-2',5'-dideoxyuridine (AIU), in the treatment of experimental ocular herpes simplex (acute and chronic epithelial and stromal keratitis and uveitis), encephalitis, and cutaneous and genital herpes infections will be evaluated by clinical, virologic and histopathologic means. Determination of aqueous, cerebrospinal fluid and serum levels of AIU following systemic administration will be made, and in vitro studies of the peak drug levels equivalent to those noted will be performed. The effect of AIU on recurrence rates of ocular herpes keratitis and its effect on the persistence of latent virus in the trigeminal ganglion will be determined. Toxicologic, teratologic, and, when appropriate, in vivo therapeutic efficacy studies of other compounds in this family are proposed. In addition to AIU, the drugs under immediate consideration are 5-iodo-5'-amino-2',5'-dideoxycytidine (AIC), 5'-amino-5' deoxythymidine (ATdR), and 5-trifluoromethyl-5'-amino-2', 5'-dideoxyuridine (AF3U). AIU has been shown in prelminary studies to have in vitro an in vivo antiherpetic activity comparable to IdUrd but without demonstrable cytotoxic or teratologic side effects. AIU's lack of toxicity and specificity of action are related to the observation that a key step in its metabolism is mediated by a herpes simple specific enzyme system. Other drugs in this family have similar therapeutically important properties. Bulk synthesis of these compounds for animal studies is proposed. This proposal will make possible the expansion of these studies to include evaluation of the therapeutic and toxicologic properties of the compounds.

BIBLIOGRAPHIC REFERENCES: Park, N.H., Pavan-Langston, D., McLean, S.L., Albert, D.M.: Therapy of experimental herpes simplex encephalitis with Aciclovir in mice. Antimicrob. Agents Chemother. 15:775, 1979. Pavan-Langston, D., Park, N.H., Lass, J.: Herpetic ganglionic latency: Aciclovir and Vidarabine therapy. Arch. Ophthalmol. 97:1508, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Eye Inst. $164,646

3.0012, RESPONSE TO THERAPY OF CUTANEOUS HERPES SIMPLEX

I.M. Freedberg, Beth Israel Hospital, *330 Brookline Ave., Boston, Massachusetts* 02215 (N01AI52530 (CONTRACT))

To study the natural history and response to therapy of facial mucocutaneous herpes simplex. Using a double-blind technique, two agents adenine arabinoside and disodium phosphoacetate and placebo will be evaluated in 150 'normal' and 75 immunocompromised patients.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $32,655

3.0013, VIRAL DISEASES OF THE ORAL CAVITY (VIDOC)

J.C. Drach, University of Michigan, Ann Arbor Campus, School of Dentistry, *Ann Arbor, Michigan* 48104 (P50 DE 02731-130028)

The program is involved in studying the basic biochemistry of model herpes simplex virus (HSV)-infected cell cultures and investigating the mode of action of selected antiviral drugs. Other in vitro studies involve the transport of antiviral drugs through the skin and the development of delivery systems that will enhance their cutaneous penetration. The pathogenesis of HSV infections of the oral and perioral regions also is being investigated. The combined objective of the basic and clinical studies is to derive effective chemotherapy for the control of HSV-induced cutaneous lesions and to evaluate these drugs clinically against herpes labialis.

The specific aims of the three portions of the program are as follows: 1) To study the mode of action of known as well as promising antiviral compounds utilizing mammalian cell cultures, HSV-infected cell cultures, and biochemical model systems. Emphasis is divided between drug action studies in intact cells and comparative biochemical studies on HSV-induced and cellular enzymes. 2) To study the derived knowledge to the development of topical drug delivery formulations.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

3.0014, VIRAL DISEASES OF THE ORAL CAVITY - DRUG DELIVERY SYSTEMS

G.L. Flynn, University of Michigan, Ann Arbor Campus, School of Dentistry, *Ann Arbor, Michigan* 48104 (P50 DE 02731-130038)

This project will study the diffusion of antiviral drugs in model systems and apply the derived knowledge to the development of topical drug delivery formulations. It is anticipated that as specific relationships among drug, vehicle and skin are identified and clarified, valid formulation approaches to salivary drug delivery problems would become evident. The study would involve two phases:

Model and Concept Development: The first phase of the work will be concerned primarily with the development of quantitative in vitro drug absorption and drug delivery procedures. Hairless mouse skin, with cross-referenced experiments employing excised (cadaver) skin, will be mounted in diffusion cells. To study drug permeability from solutions, a conventional dual reservoir diffusion cell will be employed. In order to translate these results to more clinically realistic topical drug formulations, new experimental methodology will be required. A single reservoir diffusion cell will be constructed and used to follow the penetration of drugs applied directly to the stratum corneum surface of excised skin. Data generated by these collective experiments will be analyzed by physical modeling.

Formulation Development: In the second phase it is planned to incorporate the ideas from the basic studies and their physical model analysis to an overall dosage form concept. Drug delivery will remain the uppermost issue and thus the single reservoir diffusion cell will be employed to assess absorption from the finished dosage forms.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$65,626

3.0015, EXPERIMENTAL ORO-FACIAL HERPES IN ANIMALS

R.J. Klein, New York University, School of Medicine, Dept. of Microbiology, *550 1st Ave., New York, New York* 10016 (R01 DE 04958-02)

The pathogenesis of orofacial herpes simplex virus (HSV) infection in young guinea pigs was investigated. It was observed that, despite relative prolonged persistence of the virus in the skin lesions, only small amounts of virus reached the trigeminal ganglion, and that a latent HSV infection was established only in about 30% of the infected guinea pigs. Guinea pigs surviving the primary HSV infection can be reinfected with the homologous virus at the site of the primary reinoculation, despite the presence of HSV-specific serum antibodies. Young guinea pigs inoculated with HSV in the orofacial area were irradiated with UV light: no skin lesions developed, but one third of the irradiated guinea pigs with latent HSV infection, were found to harbour free HSV in trigeminal ganglia homogenates after UV exposure. The ability of several antiviral compounds to prevent the establishment of latent infection in hairless mice was investigated. Phosphonoformate, adenine arabinoside and its monophosphate were ineffective, but phosphonoacetate and mainly acycloguanosine proved to be highly effective. HSV-infected hairless mice with evidence of latent infection in spinal ganglia did not develop latent infections in the trigeminal ganglia upon reinfection in the orofacial area. The in vitro reactivation of HSV in latently infected trigeminal ganglia of mice was delayed in the presence of interferon, whereas the presence of anti-interferon serum facilated the reactivation of the latent virus.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$86,052

3.0016, ORAL HERPES SIMPLEX - AN APPROACH TO DENTAL THERAPY

G.A. Gentry, University of Mississippi, Medical Center, School of Medicine, Dept. of Microbiology, *2500 N. State St., Jackson, Mississippi* 39216 (R01 DE 05089-01)

Our objeciive is to develop chemotherapeutic tools for the treatment of oral herpes simplex. In particular, we propose synthesizing new analogs of the naturally-occurring nucleoside arabinosylthymine (araT). These analogs will contain two independent inhibitory groups, the arabinosyl moeity as the sugar, and ethyl and methoxymethyl groups instead of the 5-methyl group of araT. We will evaluate the antiviral properties of these in cell culture and in vivo against herpes simplex virus (HSV) and equine herpes virus. We will also determine the ability of the analogs to inhibit cell growth, as well as mitogen stimulation of lymphoblast transformation. Further, we will assay their teratogenic potential in hamsters.

We will explore their mechanism of action by comparing the newly-synthesized compounds with araT with respect to their ability 1) to serve as substrate for 1) the herpesviral-specified pyrimidine deoxyribonucleoside kinase (dPyK) and b) host thymidine kinase(s); and 2) inhibit DNA synthesis in herpesvirus-infected cells.

While our findings may be applicable to a variety of herpesviruses, we beleive that because of the broader specificity of the dPyK of the herpes simplex virus type 1 (the predominant oro-facial type), araT and araT-like drugs will be more effective in dental therapy of oral lesions.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$84,337

HERPES SIMPLEX VIRUS INFECTIONS - PREVENTION

3.0017, ANTIBODIES OF SALIVA AND OTHER SECRETIONS

R.J. Genco, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (R01 DE 02814-09)

Experiments are proposed to look at three parameters: (1) The immunogenicity of purified polysaccharides derived from Streptococcus mutans particularly with respect to their induction of secretory antibodies; (2) The induction of secretory antibodies by various routes and with use of various antigens; and (3) The function of secretory antibody in protection against colonization by bacteria and also against dental caries.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

3.0018, VACCINATION AGAINST ORAL HERPETIC LESIONS

B.K. Murray, Virginia Commonwealth University, School of Basic Sciences & Graduate Studies, Dept. of Microbiology, *901 W. Franklin St., Richmond, Virginia* 23284 (R01 DE 04700-03)

This project involves development of a herpes simplex virus (HSV) protein vaccine for protection against oral herpetic lesions and subsequent nervous tissue involvement. Oral HSV infections manifested either as primary gingivostomatitis or recurrent oral lesions (cold sores), have been recognized as a major dental problem for years. We propose to use the inbred BALB/c mouse strain in which oral herpetic lesions are regularly induced by swabbing abraded lip and buccal epithelial surfaces with a type 1 strain of HSV. A nucleic acid-free viral protein and/or glycoprotein vaccine preparation will be prepared and evaluated in this system. Antigen modification, using polymerized antigens and immunomodulators (pyran, poly IC) will be used in attempts to enhance the efficacy of the vaccines. Vaccine-mediated protection will be assessed by monitoring the degree of virus involvement in oral and nervous tissue, histopathology and ultrastructure of these tissues, and incidence of virus latency and recurrence. Vaccine efficacy will be correlated with various specific immunologic, humoral, and cellular proliferation and effector functions in immunized mice and matched non-immunized control animals.

BIBLIOGRAPHIC REFERENCES: Morahan, P.S., P.F. Cline, M.C. Breinig, and B.K. Murray. Effect of pyran on latency following herpes simplex virus infections. Antimicrob. Agents Chemother. 15:547-553. 1979. Zenda, S.S. and B.K. Murray. The effect of defective interfering particles of HSV type 1 in oral infection. National Student Research Forum (Gavelton, TX). p. 66, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$80,463

3.0019, IONTOPHORESIS OF ARA-AMP TO HERPES VIRUS LESIONS

J.M. Hill, Medical College of Georgia, School of Medicine, Dept. of Cellular & Molecular Biology, *1459 Gwinnett St., Augusta, Georgia* 30902 (R01 DE 04917-02)

Our specific aims for the second year of the grant are as follows: To determine the therapeutic efficacy of iontophoretic application of Ara-AMP to HSV-2 skin lesions in hairless mice. To determine the therapeutic efficacy of iontophoretic application of Ara-AMP to HSV-2 vaginitis in NCI-Swiss-Webster mice. To perform tissue analyses on rabbits which have been infected with HSV-1, developed herpetic keratitis, and recovered.

In these three groups of experiments we will have animals which will be untreated as well as treated topically with Ara-A, IDU, and Ara-AMP.

BIBLIOGRAPHIC REFERENCES: Park, N.H., L.P. Ganarosa, B.S. Kwon, and J.M. Hill. Iontophoretic application of adenine arabinoside monophosphate (ara-AMP) to HSV-1 infected hairless mouse skin. Antimicrob. Agents Chemother. 14: 605-608, 1978. Gangarosa, L.P., N.H. Park, B.C. Fong, D.F. Scott, and J.M. Hill. Conductivity of drugs used for iontophoresis. Pharm. Sci. 67: 1439-1443, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$75,552

3.0020, IMMUNITY IN ORAL HERPESVIRUS INFECTION

S.C. Specter, Albert Einstein Medical Center, *York & Tabor Rds., Philadelphia, Pennsylvania* 19141 (R23 DE 04419-02)

The ability of Herpes simplex virus type 1 (HSV1) to cause lesions of the oral cavity is well established. This has made the oral cavity the primary target for investigations concerning the site of latent HSV1 and the level of immune competence of the host. The existing reports on the interaction of herpesvirus and the host response have established that both humoral and cellular immunity participate in control of infection by this virus. However, the state of immunity of patients with herpes has not been examined in vitro, where humoral and cellular responses can be studied in the absence of 'host' factors. In such a system the true picture of interaction between HSV1 and immunocompetent cells can be examined.

This study will examine immunoresponsiveness of peripheral blood lymphocytes from patients seen in a dental clinic. The role of dental disease in modifying host responses to herpes virus will be investigated by determining the immune reactivity of patients with various forms of oral inflammatory diseases to herpes and other antigens. This will involve testing at two levels: first to determine the nature of the response, i.e., whether humoral and/or cellular; then to determine the effect of the virus on the ability of the patients' lymphoctyes to respond in vitro to a 'third party' antigen employing the Marbrook culture system. In this manner patients with periodontal or endodontal pathologies (where there is a heightened local inflammation) will be examined to determine if they respond immunologically, on a systemic level, in a manner similar to normal patients. A third population, immunosuppressed individuals, will be examined also for their responses to HSV1.

Since previous reports show differences in the nature of the immune response to HSV1 in experimental animals as compared to humans, the present study will also include a comparison of the responses in the mouse to that seen in man.

BIBLIOGRAPHIC REFERENCES: Specter, S., Throm, R., Strauss, R. and Friedman, H. Rapid detection of bacterial growth in blood samples by continuous-monitoring electrical impedance apparatus. J. Clin. Micro. 6: 489-493, 1977. Specter, S., Bendinelli, M., Ceglowski, W.S. and Friedman, H. Macrophage induced reversal of immunosuppression by leukemia viruses. Fed. Proc. 37:57-61, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

3.0021, MATERNAL MALNUTRITION

G.T. Laven, University of Alabama in Birmingham, School of Dentistry, Inst. of Dental Reserch, *1919 7th Ave. S., Birmingham, Alabama* 35233 (R23 DE 05006-01)

Protien-calorie malnutrition has been associated with a variety of immunologic abnormalities and maternal malnutrition has been shown to adversely affect fetal organ growth. The proposed investigations explore the hypotheses that maternal malnutrition affects the immune status of the infant and that maternal secretory immunity is affected by malnutrition.

Maternal nutritional status will be evaluated by history, anthropometry, including skin-fold compressibility, and biochemically, including urea nitrogen/creatinine ratios.

Infant immune status will be assessed by measuring E-rosette formation, lymphocyte response to PHA, serum and salivary immunoglobulins, complement, antibody response and skin testing.

Maternal secretory immunity will be assessed by measuring milk levels of complement, immunoglobulins, and lysozyme, and salivary and milk antibody response to antigenic stimulation with oral Streptococcus mutans, and intestinal Salmonella enteritidis.

The protective effects of maternal milk antibody activity will be observed in infants exposed to an environmental pathogen (Salmonella enteritidis) prior to breast feeding.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$30,015

3.0022, IMMUNITY IN ORAL HERPESVIRUS INFECTION

S.C. Specter, State University System of Florida, University of South Florida, School of Medicine, Dept. of Medical Microbiology, *4202 Fowler Ave., Tampa, Florida* 33620 (R23 DE 05642-01)

The ability of Herpes simplex virus type 1 (HSV1) to cause lesions of the oral cavity is well established. This has made the oral cavity the primary target for investigations concerning the site of latent HSV1 and the level of immune competence of the host. The existing reports on the interaction of herpesvirus and the host response have established that both humoral and cellular immunity participate in control of infection by this virus. However, the state of immunity of patients with herpes has not been examined in vitro, where humoral and cellular responses can be studied in the absence of ‘host‘ factors. In such a system the true picture of interaction between HSV1 and immunocompetent cells can be examined.

This study will examine immunoresponsiveness peripheral blood lymphocytes from patient seen in a dental clinic. The role of dental disease in modifying host responses to herpes virus will be investigated by determining the immune reactivity of patients with various forms of oral inflammatory diseases to herpes and other antigens. This will involve testing at two levels: first to determine the nature of the response, i.e, whether humoral and/or cellular; then to determine the effect of the virus on the ability of the patients' lymphocytes to respond in vitro to a ‘third part‘ antigen employing the Mabrook culture system. In this manner patients with periodontal or endodontal pathologies (where there is a heightened local inflammation) will be examined to determine if they respond immunologically, on a systemic level, in a manner similar to normal patients. A third population, immunosuppressed individuals, will be examined also for their responses to HSV1.

Since previous reports show differences in the nature of the immune response to HSV1 in experimental animals as compared to humans, the present study will also include a comparison of the responses in the mouse to those seen in man.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $13,877

RECURRENT APHTHOUS ULCERS & OTHER MUCOCUTANEOUS DISORDERS

- EPIDEMIOLOGY

3.0023, APHTHOUS STOMATITIS AND BEHCET'S SYNDROME

D.L. Peavy, Baylor College of Medicine, School of Medicine, Dept. of Microbiology & Immunology, *1200 Moursund Ave., Houston, Texas* 77025 (N01DE72400 (CONTRACT))

This project is a study into the immunopathogenesis of Recurrent Aphthous Stomatitis and Behcet's Syndrome, which will include: measurement of in vitro immune responsiveness of RAS and BS lymphocytes to oral mucosal antigens; determination of tissue specificity of lymphocyte-epithelial cell interactions; investigation of possible bacterial causes of BAS, paritcularly Streptococcus sanguis; and determination as to whether lymphocytes of RAS and BS patients are thymusderived (T) or bone marrow-derived (B). The objectives are: to extend and attempt to confirm previous studies as well as to include Behcet's disease, and to determine whether or not a significant correlation exists between the immunological events observed during each exacerbation and whether or not the degree of reactivity correlates with the severity of the disease.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $69,412

3.0024, RECURRENT APHTHOUS STOMATITIS AND BEHCET'S SYNDROME

R.S. Rogers, Mayo Foundation, *200 1st St. S.W., Rochester, Minnesota* 55901 (N01DE82414 (CONTRACT))

This project is a study into the immunopathogenesis of Recurrent Aphthous Stomatitis (RAS) and Behcet's Syndrome (BS) to measure in vitro the immune responsiveness of lymphocytes from RAS and BS patients in relation to the severity and stages of the disease, determine if peripheral blood lymphocytes from RAS and BS patients are responsive to oral epithelial antigens and S sanguis antigens and determine whether lymphocytes of RAS and BS patients are thymus-derived (T) or bone marrow-derived (B). The objectives of the present solicitation are to extend previous studies and to include Behcet's disease, and to determine whether or not a significant correlation exists between the immunological events observed during each exacerbation and whether or not the degree of reactivity correlates with the severity of the disease.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $103,825

3.0025, RECURRENT APHTHOUS STOMATITIS AND BEHCET'S SYNDROME

J.S. Greenspan, University of California, San Francisco Campus, School of Dentistry, Dept. of Oral Biology, *551 Parnassus Ave., San Francisco, California* 94122 (N01DE82415 (CONTRACT))

Study the immunopathogenesis of recurrent aphthous stomatitis (RAS) and behcet's syndrome (BS) to: measure in vitro the immune responsiveness of lymphocytes from RAS and BS patients in relation to the severity and stages of the disease; determine if peripheral blood lymphocytes from RAS and BS patients are responsive to oral epithelial antigens and S. sanguis antigens; and determine whether lymphocytes of RAS and BS patients are thymus-derived (T) or bone marrow-derived (B). The present objectives are to: extend previous studies and include Behcet's disease; and determine whether or not a significant correlation exists between the immunological events observed during each exacerbation and whether or not the degree of reactivity correlates with the severity of the disease.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $120,135

RECURRENT APHTHOUS ULCERS & OTHER MUCOCUTANEOUS DISORDERS

- ETIOLOGY

3.0026, IMMUNOLOGICAL RESPONSE TO OPPORTUNISTIC FUNGI

N.N. Pearsall, University of Washington, School of Medicine, Dept. of Microbiology & Immunology, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (P50 DE 02600-130015)

The immunological response to opportunistic fungi is being studied, using Candida albicans as a model. Candida is injected into the mouse thigh; the thigh size provides an indicator of the extent of the resulting lesion. Our results show that a primary infection with Candida results in an abscess with little or no evidence for an active cell-mediated immune (CMI) response. Passive transfer of lymphoid cells has failed to transfer immunity in this system. The infected mice develop delayed hypersensitivity to Candida antigens, and specific humoral antibodies are produced. Humoral antibodies can transfer demonstrable immunity to C. albicans.

The adherence of C. albicans to buccal epithelial cells is being studied. Adherence is more marked in the presence of normal saliva than in saline. Increased adherence is correlated with germ-tube formation and filament formation by the fungi. Specific anti-candida antibodies in saliva can interfere with adherence. The adherence of C. albicans to buccal epithelial cells is being compared in three groups: normal, noninfected subjects; candida-infected carriers without evidence of candidiasis; and subjects with candidiasis. The effects of salivary antibodies on adherence are also being studied in the three groups.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $24,856

3.0027, CLINICAL ASPECTS AND EFFECTS OF TREATMENT ON HOST PARASITE INTERACTIONS OF CANDIDA ALBICANS

J.B. Epstein, University of Washington, School of Dentistry, Dept. of Oral Diagnosis, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P50 DE 02600-130033)

Oral Candidiasis is a common intraoral problem. It frequently presents as a chronic recurring infection in spite of the availability of relatively specific antifungal drugs. This study is concerned with oral candidiasis, salivary immunoglobulins and response to treatment. Patients will be examined clinically and specimens acquired prior to therapy immediately after and again two weeks after completion of therapy with mycostatin oral suspension (Squibb). A standardized examination and recording of clinical findings will be made. Whole saliva will be collected by expectoration. Mucosal swabs of clinically involved areas will be utilized in culture and identification of Candida albicans, measurement of anticandida immunoglobulins, IgG, IgA, and IgM titers, and testing of antibody influence on adherence of Candida to mucosal epithelial cells. Swabs will provide specimens for cultures for the presence of the organism in clinically identified areas of infection and smears for evaluation of the presence of filamentous forms. Candidiasis will be determined with clinical evidence, smear, and culture evidence. Response to treatment will be studied. The results will be interpreted in terms of: 1. Salivary antibodies specific for Candida albicans in control, carrier, and infected populations. 2. Salivary antibody changes with treatment. 3. The role of mucosal adherence of Candida albicans in Candidiasis. 4. Role of salivary IgA in adherence of candida to mucosal epithelial cells in the study of populations. 5. Role of salivary IgA and adherence and response to treatment.

This investigation of a possible oral defense mechanism in oral candidiasis, its relationship with disease and carrier state, as well as the effect of antifungal medication, may significantly increase our knowledge and ability to treat the condition successfully.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$64,294

3.0028, FACTORS DETERMINING VARIATION IN ADULT ORAL MUCOSA

I.C. Mackenzie, University of Iowa, School of Dentistry, Dept. of Periodontology, *Jessup Hall, Iowa City, Iowa* 52240 (R01 DE 05190-01)

Oral mucosa shows a marked regional variation in structure and such variation appears to be related to regional differences in function. similar pattern of variation is seen in the skin. Epithelia are continuously regenerating structures. There is some evidence to suggest that a continuous influence of the subepithelial connective tissue is required to maintain regional specificity of structure.

Many of the adverse pathological processes occurring in the oral cavity, ranging from periodontal disease to carcinoma are associated with, or are causally related to, changes in the maintenance of epithelial structure and information which leads to an understanding of this process would be of great value. As working hypotheses, we propose a) that epithelial maintenace can be considered in relation to the control of three types of cellular activity; rates of synthesis, types of synthesis and establishment of tissue architecture and b) that a basic pattern of epithelial cell differentiation is continuously modulated by the subepithelial connective tissue into a site specific pattern of organization.

The objectives of the proposed research are to evaluate whether: a) all epithelia have the same basic pattern of differentiation, b) there is a regional specificity of the connective tissue, c) all epithelia are capable of remodulation, d) the organization, rate and type of epithelial synthesis are independently controlled and e) there is a specific cell type responsible for the role of maintaining epithelial integrity and specificity. We propose to investigae this problem using separation techniques which we have recently developed to examine a selected, diverse range of oral epithelial and epidermal specimens following both homotypic and heterotypic transplantation of epithelium and connective tissue into protected sites in histocompatible mice and to evaluate the results by examining the effects of such tissue interchanges on morphological structure, rates of cell production and patterns of synthesis of different types of keratin and cell surface materials.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$87,175

3.0029, LATENCY OF HERPES SIMPLEX IN ORO-FACIAL INFECTIONS

A.J. Nahmias, Emory University, School of Medicine, Dept. of Pediatrics, *1364 Clifton Rd. N.E., Atlanta, Georgia* 30322 (R01 DE 05194-01)

A major clinicoepidemiological problem associated with Herpes simplex viruses (HSV) is that of recurrent infections. Current evidence indicates one of the major sites for latency in-between recurrences is the sensory ganglion. The proposed studies are aimed at obtaining further understanding of the basic mechanisms of HSV-1 latency in human trigeminal ganglia. Single cell type preparations of neuron cells and supporting cells will be used to define and enumerate the cells harboring the virus. The possible presence of Ig or Fc Ig receptors on the membrane of the different cell preparations, which might modulate virus reactivation, will be ascertained. Several methods will be employed to determine whether reactivation of virus from latency is influenced by the cell's metabolism and/or the status of the virus genome. These include: a) comparing the ability of HSV and poliovirus to replicate in freshly explanted cells or cells in culture for several days; b) the effect of cyclic nucleotide (cAMP and cGMP) enhancers, depolarizing factors, e.g. ouabain, and ts mutants to accelerate virus reactivation from latency. Information obtained from these studies should be applicable to HSV-2 and the infections produced by this virus type. The long-term goal is to find some means of preventing HSV recurrences which afflict at least one-third of our population and may, on occasion, be associated with severe disease.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $62,462

3.0030, NUTRITIONAL MODULATION OF ORAL MUCOSAL PERMEABILITY

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The maintenance of an effective epithelial barrier, which can minimize the penetration of toxic byproducts from the microbial flora into the connective tissue, represents one of the most important mechanisms in the resistance of the host to infection. We have previously observed that the basement membrane represents the rate-limiting barrier to the penetration of non-Keratinized mucosal epithelium by bacterial endotoxin and, more recently, inulin and dextran. We have also noted that acute ascorbate deficiency can increase mucosal permeability to these three agents.

Current studies focus on the effects of acute folate and Vitamin deficiency on oral mucosal permeability to dextran (MW 70,000), and also on the effects of these deficiencies on basement membrane biosynthesis. In addition, static, autoradiographic studies have suggested that the mucosal barrier may possess 'directionality.' That is, the speed of penetration may depend upon the direction of penetration. This observation is currently being evaluated in a dynamic permeability assay system.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

3.0031, HERPES SIMPLEX INFECTIONS IN CANCER CHEMOTHERAPY PATIENTS

K.H. Rand, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Gainesville, Florida* 32601 (573-001-I)

It is well known clinically that patients undergoing intensive cancer chemotherapy are susceptible to unusually prolonged and severe Herpes simplex virus (HSV) infections, generally involving the oral mucous membranes. Similar prolonged infections are also commonly observed in renal and cardiac transplant patients in the first 2 months following transplantation. We plan to study the occurrence of oral mucous membrane HSV infection in relationship to the cycle of chemotherapy. Thus, by culturing the oral secretions 2-3 times/week during an entire cycle of chemotherapy, we may ultimately be able to determine the relationship between the chemotherapy induced immunosuppression and the interval to first positive mouth culture and to duration of viral shedding. In addition, if certain drugs or combinations appear to directly reactivate HSV, this should also become apparent. Results so far show 8/113 HSV antibody positive patients who had received cytotoxic chemotherapy within the past 60 days (most within the past 30 days) had a positive mouth culture for HSV, whereas only 1/89 patients with malignancy, but receiving no chemotherapy were positive for HSV (p equals .04, Fisher's exact probability). Too few patients have been studied prospectively to draw conclusions, but preliminary data indicate a subgroup who do develop severe oral mucous membrane lesions and prolonged viral shedding, the onset of which suggests the chemotherapy itself may directly trigger viral reactivation.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

3.0032, ORAL CARCINOGENESIS, VITAMIN A AND RETINOIDS

G. Shklar, Harvard University, Boston Campus, School of Dentistry, Dept. of Oral Medicine & Oral Pathology, *188 Longwood Ave., Boston, Massachusetts* 02115 (1169 (M) R1)

The objectives of the proposal are to determine whether vitamin A or the synthetic retinoids administered systemically can act to delay or inhibit carcinogenesis of oral mucous membrane and if so, through what mechanism. Two well-established oral mucosal tumor systems will be used - the hamster buccal pouch epidermoid carcinoma induced by painting with DMBA in oil, and the hamster tongue epidermoid carcinoma induced by painting with DMBA in acetone. Delayed carcinogenesis will be evaluated histologically by delayed appearance of dysplasia, carcinoma in situ and invasive epidermoid carcinoma. Retinoids used will be vitamin A, 13-cis-retinoic acid, retinyl acetate, and retinyl palmitate. Labelled retinoids will be used to determine whether systemically administered retinoids can be found in oral mucosa. Hemagglutination assay and PHA assays will be used to test for possible enhancement of cell-mediated immunity in the retinoid animals.

SUPPORTED BY
Council for Tobacco Research
U.S.A. Inc. $48,093

RECURRENT APHTHOUS ULCERS & OTHER MUCOCUTANEOUS DISORDERS

- PATHOLOGY

3.0033, DIAGNOSTIC AND PROGNOSTIC FEATURES IN THE HISTOPATHOLOGY OF ORAL MALIGNANT AND PREMALIGNANT MUCOSAL LESIONS

N.W. Johnson, University of London, London Hospital Medical College, Dept. of Oral Pathology, *Turner St., London E1 2AD, England, United Kingdom*

The aims of the study are to determine which clinical and histopathological features of oral cancer have diagnostic and prognostic value. A range of clinical and microscopic features (23 related to the epithelium and 16 related to connective tissue) has been scored from 100 cases with at least 5-year follow-up, using specially devised semiquantitative scales, and analyzed for correlation with patient survival and behavior of the tumor, using a computer. The work is continuing but preliminary results indicate that host immune inflammatory response as seen in tumor stroma is at least as important as epithelial features in predicting survival. Factors such as mitotic activity and degree of keratinization, traditionally given great weight in grading epithelial neoplasms, do not appear to be of great prognostic value.

SUPPORTED BY

University of London	funds n.a.

RECURRENT APHTHOUS ULCERS & OTHER MUCOCUTANEOUS DISORDERS

- DIAGNOSIS & TREATMENT

3.0034, THE NATURE OF PEMPHIGUS ANTIGEN

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No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$4,084

RECURRENT APHTHOUS ULCERS & OTHER MUCOCUTANEOUS DISORDERS

- PREVENTION

3.0035, LYMPHOCYTE FUNCTION IN RECURRENT APHTHOUS ULCERATION

J.S. Greenspan, University of California, San Francisco Campus, School of Dentistry, Dept. of Oral Medicine/Hospital Denistry, *551 Parnassus Ave., San Francisco, California* 94122 (R01 DE 04736-02)

Recurrent aphthous ulceration (RAU) is a common but troublesome chronic disease. The cause is unknown, although immunological factors have been implicated. Circulating antibody to fetal oral mucosa has been found, suggesting an autoimmune antibody-mediated mechanism. However, this antibody does not appear to be directly cytotoxic. There is also evidence suggesting a role for lymphocytotoxicity in the pathogenesis of the disease. However, recent studies suggest a mild impairment of cellular immunity.

It is suggested that the pathogenesis of RAU involves a complex interaction between antibody, lymphocytes and the target tissue. Current concepts of immunological homeostasis postulate a balance between effector and regulatory mechanisms. Aspects of RAU which may reflect both of these mechanisms will be studied. Antibody-dependent cellular cytotoxicity (ADCC) has been implicated in the pathogenesis of several autoimmune diseases. Specific ADCC mechanisms will be evaluated in patients with RAU and controls. Several laboratories have recently shown that subtle defects in T-cell function can be demonstrated by stimulation of peripheral blood lymphocytes using suboptimal doses of phytohemagglutunin (PHA). A PHA dose-response assay with RAU patients' lymphocytes will be used to measure the presence and extent of this T-cell dysfunction.

BIBLIOGRAPHIC REFERENCES: Evaluation of culture techniques for guinea pig oral mucosa. F.P. Grimaldi, B.L. Cullen & J.S. Greenspan. AADR March 1979. J. Dent. Res. 58:Sp. Iss.A, January, 1979 0455.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$65,741

3.0036, HUMAN ORAL MUCOSA IN VITRO - SUBSTRATE INTERACTIONS

J.H. Lillie, University of Michigan, Ann Arbor Campus, Medical School, Dept. of Anatomy, *1335 E. Catherine St., Ann Arbor, Michigan* 48104 (R23 DE 04945-02)

A study of human and primate oral epithelium in vitro is proposed. Two basic culture techniques, primary cell outgrowth and primary cell suspensions, will be studied using varying conditions, temperatures and sera. Once optimal conditions are selected for the short-term culture of human and primate oral epithelium, cells will be cultured on a variety of carefully defined connective tissue substrata including types I and III collagen gels, collagen - proteoglycan gels and an in vitro formed basal lamina (Descemet's membrane). The collagens will be extracted and purified under conditions designed to maintain the integrity of the native molecule. Collagen gels will be formed under physiologic conditions of pH, ionic strength and temperature. The interaction of epithelial cells with the various substrata will be assessed in a variety of ways (cell aggregation, migration and growth characteristics) in addition to a detailed phase microscopic -ultrastructural study of the cell - substratum interface. These studies will be undertaken to determine whether epithelial cells grown in culture on defined 'physiological' substrata will interact with them in fashions which are similar to epithelial-connective tissue interactions observed in vivo.

Principle methodologies to be employed include: cell culture, phase and electron microscopy, a variety of extraction techniques and gel electrophoresis.

BIBLIOGRAPHIC REFERENCES: Occhino, J.C., L.J. Scaletta, D.K. MacCallum, and J.H. Lillie. Isolation and immunological identification of basement membrane zone antigens from human skin. Lab. Invest. 39:1-9, 1978. Tandler, B., J.H. Lillie and D.K. MacCallum. Cytoplasmic Crystalloids in rat parotid glands. Archs. Oral Biol., in press, 1978.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $22,018

3.0037, ULCERATIVE LESONS AND TUMORS - APHTHOUS ULCERS - CLINICAL TRIALS

E.A. Graykowski, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Laboratory of Oral Medicine, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00094-06 LOM)

The object of this project is to study the etiology and pathogenesis of mucosal diseases of the oral cavity, with the ultimate goal of treatment and prevention. At the present time, emphasis is on recurrent aphthous ulcers. A protocol was completed, and the results strongly suggest that mechanical trauma may be one of the precipitating factors in recurrent aphthous ulcers.

BIBLIOGRAPHIC REFERENCES: Graykowski, E.A.: Aphthous-Behcet's Syndrome Workshop. Double-Blind trial of tetracycline in recurrent aphthous ulceration. J. Oral Path. 7:736-382, 1978. Graykowski, E.A., et. al.: Appendix II, Aphthous Stomatitis-Behcet's Syndrome Workshop. Treatment of recurrent aphthous ulcerations. J. Oral Path. 7:439-440, 1978.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $211,620

TUMORS OF THE ORAL MUCOSA & CONNECTIVE TISSUES - EPIDEMIOLOGY

3.0038, CANCER INCIDENCE IN RELATION TO ASBESTOS IN DRINKING WATER IN THE PUGET SOUND REGION

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A high level of asbestos, occurring naturally, has been found in drinking water in Seattle, Everett, and other nearby areas. Cancer incidence and mortality rates for areas with different water supplies will be calculated. Control factors will include age, sex, race, and socioeconomic status. Sites of interest are gastrointestinal tract, mouth and esophagus, pancreas, and urinary tract. Other control sites will be examined throughout the analysis. Various sub-studies will be included.

SUPPORTED BY
(No Supporting Organization
Reported) funds n.a.

3.0039, EPIDEMIOLOGY OF ORAL CANCER

S.L. Fischman, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Medicine, *3435 Main St., Buffalo, New York* 14214 (D-IARC-79-919)

A case-control study of the various nutritional and dietary factors common to patients with cancer of the oral cavity is in progress. Data on oral hygiene, use of dental prostheses, smoking, and alcohol consumption are also being obtained. Both self-administered questionnaires and interviews are used. For interim results see J. Nat. Cancer Inst. 59 (6): 1611-18, 1977.

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Reported) funds n.a.

3.0040, TRI-COUNTY STUDY OF CANCER OF THE MOUTH, OESOPHAGUS, PHARYNX, LARYNX, STOMACH, COLON AND RECTUM

S. Graham, State University of New York, Buffalo Campus, School of Arts & Letters, Dept. of Sociology/Social & Preventive Medicine, *3435 Main St., Buffalo, New York* 14214 (D-IARC-79-920)

There have been suggestions that diet, alcohol ingestion, oral conditions, and smoking are related to cancer of the mouth, oesophagus, and stomach, and that alcohol ingestion and smoking are related to cancer of the larynx. These relationships are the subject of this inquiry. To avoid hospital related bias and to obtain detailed information on each case, all new cases in Erie, Niagara and Monroe Counties in New York State will be interviewed. It will take four years to obtain enough (about 300) cases of cancer of the oesophagus and larynx for males, and two years to obtain the buccal and stomach cancer cases necessary for analysis. Cancers of the oesophagus and larynx are so rare in females that the inquiry will be limited to buccal and stomach cancer among females. All controls will be matched on age (within five years) and sex and reside in the neighborhoods of the cases. To obtain all corroborative evidence possible as to dietary habits of subjects, spouses or other individuals who live with or cook for the subjects will be interviewed. A multivariate analysis of the results will be carried out. Data collection has proceeded well in the past year. We have interviewed 744 cases, comprised of 161 mouth, 97 oesophagus, 169 larynx, 28 pharynx, 141 stomach, 111 colon, and 37 rectum cancers. In addition, 599 controls, 112 control spouses and 119 case spouses have been interviewed. Data collection will continue as scheduled over the next year. Preliminary analysis of 100 case/spouse and 100 control/spouse pairs to determine extent of agreement with regard to the subjects' dietary habits is under way.

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Reported) funds n.a.

3.0041, SMOKING AND CHEWING HABITS IN RELATION TO HEALTH - A PROSPECTIVE STUDY IN BOMBAY

K. Jayant, Cancer Research Inst., Epidemiology Div., *Dr. Ernest Borges Marg, c/o Tata Memorial Ctr., Bombay 400012, Maharashtra, India* (D-IARC-79-261)

A number of retrospective studies carried out in this country have demonstrated the association of smoking and chewing habits with oral and pharyngeal cancers. Laboratory and experimental studies on bidi smoke and betel quids have also served to establish this cause-effect relationship. To see whether the results obtained in retrospective studies are sustained in prospective studies in which large populations with known habits are followed for several years for the occurrence of cancer, a limited study of this nature has been in progress, following earlier pilot studies. About 7,000 white-collar workers and 3,500 blue-collar workers over the age of 35 have been followed up for varying periods since 1969. A preliminary analysis of the data on white collar workers is being undertaken.

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Reported) funds n.a.

3.0042, EPIDEMIOLOGICAL ASPECTS OF A CANCER CONTROL PILOT PROJECT

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Within the framework of a program for the early detection of precancerous lesions and early cancer of the uterine cervix, oral cavity, and pharynx, by systematic clinical examination, cytology and biopsy, aetiological and epidemiological studies will be undertaken. The prevalence and incidence of these cancers will also be assessed. Knowledge, attitudes and practices relating to cancer are being examined in relation to a large number of factors including age, sex, religion, occupation, income, etc. Questions are asked about diet, personal habits, reproduction associated factors, etc.

SUPPORTED BY
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Reported) funds n.a.

3.0043, NATIONAL REGISTRY OF ORAL PRECANCEROUS CONDITIONS

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Preliminary studies indicate that as in oral carcinoma, there is predominance of Indian patients (72 percent) with oral precancerous conditions (OPC). OPC also seem to be closely related to oral habits. The peak age incidence was between 51-60 years (40 percent). The distribution of OPC was: (1) homogeneous leukoplakia (51.2 percent), (2) lichen planus (16.1 percent), (3) oral submucous fibrosis (15.2 percent), (4) speckled leukoplakia (11.9 percent), (5) erythroplakia (2.8 percent) and (6) smoker's keratosis (2.8 percent). Seventeen patients (8.8 percent) had two OPC, Indian females forming the largest part of this group (59 percent). Of these 17 patients, 76.5 percent had submucous fibrosis (SMF) and leukoplakia. In Malaysia so far no case of SMF has been reported in Chinese or Malayan males. The WHO premalignancy index (PMI) score distribution was as follows: (a) 21.4 percent, (b) 31.7 percent, (c) 37.2 percent, and (d) 9.7 percent. The most common sites for OPC were (1) buccal mucosa (65 percent), (2) tongue (13 percent) and (3) labial commissures (9 percent). The labial commissures (85 percent), tongue (47 percent) and the buccal mucosa (43 percent) had the most ominous precancerous histological features. Similarly, the most ominous precancerous histological features (PMI) scores of (c) and (d) seen in the various OPC were: (1) erythroplakia (75 percent), (2) speckled leukoplakia (65 percent), (3) SMF (56 percent) and (4) homogeneous leukoplakia (48 percent); SMF is an important precancerous condition in the Indians. The cause of SMF is unknown and there is also no known treatment for this condition. This limited study so far indicates that oral lichen planus, smoker's keratosis, and white spongy naevus of the floor of the mouth do not appear to be precancerous conditions in Malaysians as they have been reported to be in population studies elsewhere. The differences could be largely due to the different patterns of oral habits.

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Reported) funds n.a.

3.0044, AN INVESTIGATION INTO THE SO-CALLED PREMALIGNANT LESIONS OF THE ORAL CAVITY

C.W. van Wyk, University of Stellenbosch, Faculty of Dentistry, Dept. of Oral Pathology, *Private Bag 11, Tygerberg 7505, Cape Province, South Africa* (D-IARC-79-491)

The object of the study is to determine the prevalence, the anatomical distribution, the histopathology, the ultrastructure and histochemistry of the so-called premalignant oral lesions (leukoplakias) among different population groups in Cape province (Bantu, colored, white and Asian) paying due regard to habits, social circumstances and geographical distribution. Furthermore, a similar demographic study is being carried out on oral squamous carcinomas among the same people to make comparisons between the premalignant and malignant lesions possible. In addition all other oral mucosal lesions detected during the survey are recorded and their distribution plotted. Specific investigations are undertaken into the etiology of some, especially the atrophic lesions and lesions caused by viral infections.

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Reported) funds n.a.

3.0045, EPIDEMIOLOGY AND PATHOLOGY OF CANCER IN MALAWI

M.S. Hutt, University of London, St. Thomas Hospital Medical School, Dept. of Morbid Anatomy, *Lambeth Palace Rd., London SE1 7EH, England, United Kingdom* (D-IARC-79-627)

All pathological specimens from Malawi for the last 10 years have been examined in St. Thomas' Hospital Unit of Geographical Pathology. Analyses of the epidemiological features of Kaposi's sarcoma and of precancerous and cancerous lesions of the conjunctiva have been completed; studies of salivary gland neoplasms, malignant histiocytosis and solitary myeloma are under way.

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Reported) funds n.a.

3.0046, EPIDEMIOLOGY OF ORAL SQUAMOUS CELL CARCINOMA

N.W. Johnson, University of London, London Hospital Medical College, Dept. of Oral Pathology, *Turner St., London E1 2AD, England, United Kingdom* (D-IARC-79-629)

Over 300 cases of oral squamous cell carcinoma treated at the London Hospital Medical College are being analyzed in a case characteristics study which aims to determine high risk groups and to establish what factors affect prognosis (e.g., site, age, sex, etiology, size of lesion at presentation, rate of tumor growth and histopathological category). The study is both retrospective and prospective. A modification of the TNM grading and staging system is being evaluated. Data are analyzed using the statistical package for the social sciences with corrections for age employing both the Peto and Peto method and the Cox method.

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3.0047, EPIDEMIOLOGY OF OROPHARYNGEAL CANCER, AND ESOPHAGUS AND BREAST CANCERS

D.D. Patel, Gujarat Cancer & Research Inst., Dept. of Surgery, *New Civil Hosp. Campus Asarwa, Ahmedabad 380016, Gujarat, India*

DESCRIPTION: Oropharyngeal cancer constitutes 45% of all cancers in men. Cancer of the base of the tongue is the most common form of this cancer. The exact etiology of such high prevalence of these cancers is still unknown.

Cancer of the esophagus constitutes 8% of all cancers in men. Etiological factors causing such high prevalence are still elusive.

Cancer of the breast constitutes 20% of all cancers in females. It is thought that its incidence is higher in Bohra community, a sect of muslims.

By collecting data on epidemiology, it is desired to obtain some sensitive data to throw light on etiology.

SUPPORTED BY
Gujarat Cancer & Research Inst. funds n.a.

3.0048, MASSIVE DETECTION OF ORAL AND MAXILLOFACIAL CANCER

N.J. Lobos, PLAPO, *Jose Miguel de la Barra 475, Casilla 1903 Correo Central, Santiago, Chile*

OBJECTIVES: 1. To detect oral and maxillofacial malignant and pre-malignant lesions in the population of the metropolitan area of Santiago, Chile; 2. To put into operation a service for early diagnosis; 3. To offer these services to the public; 4. To evaluate the diagnostic methods used; 5. To obtain prevalence and incidence rates for these lesions; 6. To teach pre-graduate students at the Faculty of Odontology; 7. To register and follow-up detected cases; to refer patients to the appropriate treatment centers.

METHOD: 1. Promotion of self-examination of the oral cavity in the public; 2. Clinical examination; photography; toluidine-blue test; exfoliative cytology (specimen collection, processing and diagnosis of slides) and biopsy of suspicious lesions; 3. Tabulation and evaluation of results according to the International Classification of Diseases-Oncology.

SUPPORTED BY
Universidad de Chile funds n.a.

TUMORS OF THE ORAL MUCOSA & CONNECTIVE TISSUES - ETIOLOGY

3.0049, ORAL CANCER AND ASSOCIATED ORAL CONDITIONS

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SCOPE: To determine prevalence of submucous fibrosis, leukoplakia, and oral cancer in adults from four villages in which habits of tobacco usage vary; to record location of lesions within the oral cavity; to observe and correlate occurrence and site of oral lesions with habitual use of tobacco smoked or chewed, clinical appearance and histologic character of lesions of leukoplakia, oral cancer, and submucous fibrosis, and occurrence and site of oral lesions with other customs and habits; to establish a register of individuals with clinical leukoplakia negative for malignancy on histologic examination, and a control register of individuals for prospective study.

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3.0050, ETHANOL AND THE ETIOLOGY OF ORAL CANCER (HAMSTERS)

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This project is part of a broader program (CA 12376-08) whose summary states: This program project grant has supported an integrated multidisciplinary program in environmental carcinogenesis relating retrospective case-control epidemiological studies and experimental research. The latter includes cell culture, animal model, and human subject investigations. Proposed studies by organizational division in the forthcoming period are: 1) Epidemiology: various cancer studies in the U.S. and overseas, emphasizing GI tract and breast cancer. 2) Nutrition: endocrine-related cancer studies via hormonal effects of high-fat diets in various human populations; also dietary studies on colon carcinogenesis utilizing fecal analyses. 3) Molecular Biology and Pharmacology: study of the mechanism of the high-fat effect on breast cancer development using animal models and cell cultures; also the mechanism by which alcohol may act as a cocarcinogen in oral cavity cancer. 4) Experimental Pathology: model systems for the study of the pathogenesis of tumor development. 5) Experimental Carcinogenesis: investigation of the carcinogenic action of hydrazines, nitrosamines, and methylated polynuclear hydrocarbons, in addition to bracken fern. 6) Occupational Health and Toxicology: assessment of cancer risk to welders as a model population.

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3.0051, ORAL FLORA AND CARCINOGENESIS OF DENTAL THERAPEUTICS

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The objective of this research is to establish the role of the oral flora in affecting the host's response to possible carcinogens in the environment. Concern about exposure to possible mutagenic and carcinogenic agents has stimulated the development of test systems to warn of the presence of such compounds. Metabolic reactions of potential significance to carcinogenesis (azo, nitro, reduction; nitroso formation and degradation) will be examined to ascertain whether the oral flora is capable of playing a role similar to that of the intestinal flora as being important in the activation or deactivation of potential carcinogens. Initially dental therapeutics and tumorigenic agents in cigarettes will be tested because of their chronic exposure and application to the oral mucosa. DNA damage that may result from exposure to various dental therapeutic agents (chemicals) will be quantitated using the Ames in vitro mutagen test system. This method maximizes detection of DNA damage by Salmonella typhimurium mutants in vitro. The usefulness and sensitivity of the above in vitro method has been improved by infecting germ-free rats with the Salmonella mutant. This model incorporates bacterial metabolism and mammalian physiology by maintaining the bacterial mutants in the oral cavity and gastrointestinal tract. This is advantageous since these bacteria would then function as a biological probe, indicating the DNA damaging ability of chemicals under conditions present in the actual animal. An important advantage of this model is that the bacteria normally present in the oral cavity and gastrointestinal tract can be added into the rat in selected ways so their role in carcinogenesis (vis-a-vis mutagenesis) can be evaluated under well-controlled conditions. Using these techniques we hope to identify potential carcinogens (therapeutic agents) as mutagens and determine the role of the oral and intestinal flora in the carcinogenic process.

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3.0052, ENHANCED ORAL CARCINOGENESIS BY LOW DOSE X-RADIATION

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The tissues of the human oral cavity are frequently exposed to repeated low doses of known and suspected carcinogens such as alcohol, tobacco smoke, and x-radiation from diagnostic medical and dental radiology. Previous studies in our laboratory have demonstrated synergy between concurrent topical applications of 7, 12-dimethylbenz(a) anthracene (DMBA) and exposures to modest levels of x-radiation in hamster cheek pouch tumorigenesis. This synergy was manifested by greater tumor incidence, shorter latent period, and greater tumor volume in animals receiving combined treatments than in animals receiving either treatment alone. Radiation enhancement of DMBA lingual tumorigenesis was also observed in similar studies. We have also shown that low-level x-irradiation causes a significant, late increase in cheek pouch vascular volume and that there is a significant interaction between the effects of x-radiation and DMBA or DMBA-induced tumors on cheek pouch functional vasculature. The proposed studies would examine the effects of decreasing radiation dose on DMBA-induced tumor incidence and progression as well as the possible mechanistic role of radiation-induced hemodynamic changes in the induction and progression of these tumors. Young adult male Syrian golden hamsters will receive various doses of DMBA to the cheek pouch accompanied by repeated exposures of 1-20R x-radiation at weekly intervals. The temporal relationships between applications of chemical and radiation will vary. Animals will be observed for varying lengths of time; tumor latency, volume, incidence, histopathology, and hemodynamics will be studied using observational, histopathological, and radioisotopic distribution techniques. It is anticipated that the results of these studies will clarify dose-response relationships and time-dose relationships of low level x-radiation in this system, leading to a more quantitative base for calculations of human radiation risk estimates. Additionally, the data should provide information on the nature of radiation induced hemodynamic changes in the induction of epithelial neoplasms by low level exposures to multiple environmental carcinogens.

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Research $68,289

3.0053, CORE PROTEINS OF SALIVARY GLYCOPROTEINS

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In this year of our study, we will concentrate on the determination of the amino acid sequence of the glycopeptide repeating segments of bovine submaxillary glycoprotein. These segments, which are approximately 28 amino acids in length, constitute a family of glycopeptides whose members differ from one another in the positions of several amino acids. We have referred to these differences as homologous substitutions. The primary concern for the first part of the year will be to effect a separation of the members of the homologous glycopeptide family.

We will initially use classical chromatographic media, such as Dowex-50, Dowex-1, phosphocellulose, and ion exchange cellulose for separation. Where possible HPLC methodology will be used to obtain maximum resolution. An LKB Ultragrad will be used for non-linear gradient elution. Columns of spherical hydroxylapatite and ODS reverse phase media will also be tried.

The separated segments will then be sequenced by the Edman procedure, if necessary, using a micro-modification we have developed based on fluorescence.

Peptides obtained through beta-elimination and hydrolysis will be used to provide overlapping sequences.

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Research $0

3.0054, AGING AND OPTICAL CHANGES IN TISSUES

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Collagen and proteoglycan are considered as molecular indices to the biological aging process. This consideration is especially attractive in such tissues as tendon, where the functional constituents are little else. The aim of this research is to measure the interrelationship of these molecules directly in tendon without chemical or physical disruption. Changes are correlated with normative aging, and with retarded or accelerated aging in rats as functions of varying nutrition.

Luminescent probing is used for direct observation of tendon preparations. Information derives from ultraviolet light activated electron excited states (principally triplet, or as phosphorescence) of tail tendons supercooled to as low as 4.2 degrees Kelvin. The luminescent center in collagen is tyrosyl residues, and in proteoglycan as tryptophanyl residues. The excited states of these aromatic amino acids varies significantly. Thus each can be differentiated simultaneously.

A fully compensated spectrophotofluorimeter has been modified to handle tendon fibers in a helium refrigerator. Optical data from the instrument are discerned and denoted by a computer, and changes in quantum functions are recorded in terms of initial population of excited states and their lifetimes.

BIBLIOGRAPHIC REFERENCES: Hoerman, K.C. Nutrition and Aging: Optical Changes in Tendons, J. Nutrition, 106:28(R), 1976 (October).

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Research $0

3.0055, KERATOHYALIN IN KERATINIZATION

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Keratinized epithelium is the protective layer of the body and parts of the oral cavity. Cells of the fully differentiated layer, the stratum corneum, contain heratin filaments embedded in a matrix. Keratohyalin granules (KHG) have been proposed as the source of the matrix material. In normal keratinization of epidermis and palate, KHGs are present in cells of the s. granulosum, then disappear when these cells become cornified. KHGs are generally absent from parakeratinized or nonkeratinized portions of oral epithelium. The recently isolated stratum corneum basic protein (SCBP) may be the interfilamentous matrix material. SCBP aggregates with keratin filaments in vitro to form macrofibrils in which the filaments are highly aligned. Biochemical and immunologic evidence suggests that SCBP is derived from a higher molecular weight precursor protein in

KHGs. Our hypothesis is that SCBP is generated in vivo from the KHG precursor by a specific proteinase, and then associates with keratin filaments forming an insoluble macromolecular complex with a stabilized structure, as found in the s. corneum. This hypothesis will be tested by investigating the mechanism of formation of SCBP from its precursor, by characterizing a possible proteinase responsible for this conversion, and by studying the interaction of SCBP and keratin filaments. The significance of this interaction in keratinization of human oral mucosa will be assessed. SCBP will be tested for its ability to form macrofibrils with keratin filaments isolated from human keratinized (palate), parakeratinized (gingiva), and non-keratinized (buccal) oral epithelium. The concentration of SCBP may be correlated with the type of keratinization in normal oral tissue or with the extent of inflammation in gingivitis, a condition in which the extent of keratinization may change. Thus, variation in this keratohyalin-derived protein, SCPB, is a possible biochemical basis for morphologic differences in keratinization in human oral epithelium.

BIBLIOGRAPHIC REFERENCES: Dale, B. A., Stern, I. B., and Clagett, J. A. Initial characterization of the proteins of keratinized epithelium of rat oral mucosa. Arch. Oral Biol. 22:75-82, 1977. Dale, B. A. and Thompson, W. B. Stratum corneum basic protein of keratinized rat oral epithelia. J. Dental Res. 57:222. 1978 (Abstract).

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Research $74,180

3.0056, ENHANCEMENT OF ORAL CANCER AFTER ALLOGRAFTING

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The proposed investigation concerns itself with the observation that organ allograft recipients have a greater risk of developing squamous cell carcinoma of the labial mucosa as well as other types of cancer.

I hypothecate that the increased incidence of cancer is, at least in part, a result of the generation of suppressor cells induced by the allograft antigens and that these cells nonspecifically reduce the immune response to nascent tumors arising in the allograft recipients. This hypothesis is supported by preliminary experimental evidence presented by myself (23) and others (24).

The need for this hypothesis has been necessitated by the numerous investigations which have shed doubt on the efficacy of the classical immunological surveillance system as an explanation for the observed increased incidence of neoplasia in allograft recipients. In order to support by hypothesis, four major questions are asked in this proposal: 1. Do allografted mice have an enhancement of syngeneic tumor growth? 2. Is the anti-tumor immune respone reduced in the allografted recipients? 3. Is the reduction of the anti-tumor immune response due to suppressor cells within the spleens of the allografted mice? 4. Are the suppressor cells T cells or macrophages?

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Research $34,720

3.0057, ULCERATIVE LESIONS AND TUMORS - PAPILLOMAS OF ORAL CAVITY

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Human cutaneous and oral cavity papillomas are being examined for the presence of human papilloma virus (HPV) by an antiserum which is cross-reactive with an antigen present in all papilloma viruses. Fluorescent antibody (FA) tests are being done on frozen sections of wart tissues and peroxidase-antiperoxidase (PAP) tests are being done on sections of formalin-fixed tissue.

BIBLIOGRAPHIC REFERENCES: Jenson, A.B., Openshaw, H., Hooks, J.J., Puga, A., and Notkins, A.L.: Herpes and other virus-induced oral diseases. In Current Advances in Oral Biology, edited by Dr. H.C. Slavkin (in press) 1979.

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Research $188,872

3.0058, THE EFFECTS OF ALCOHOL AND TOBACCO ON THE HUMAN ORAL MUCOSA

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OBJECTIVE: To determine if an individual's usage of tobacco products and alcoholic beverages produces recognizable microscopic prodromata in the oral mucosa.

RESEARCH PLAN: Each human volunteer (without clinical evidence of oral mucosa changes) provided social data per questionnaire. The volunteer then submitted to an incisional biopsy of buccal mucosa under local infiltration anaesthesia and also had two areas of his oral mucosa scraped for oral exfoliative cytology examination. All specimens were numbered and processed without further identification.

METHODOLOGY: The questionnaires provided a basis for categorization into four classes: I-Non-Smoker, Non-Drinker; II-Non-Smoker, Drinker; III-Smoker, Drinker; and IV-Smoker, Non-Drinker. Each cytology smear and incisional biopsy specimen was examined by light microscopy. The social data were then combined with the histologic findings.

CONCLUSION: A total of 48 volunteers were examined. In Class I, ten of the 15 cytologies were reported completely normal. There were five atypias but the accompanying tissue biopsies revealed slight parakeratosis in only two of these. In Class II, Non-Smoker-Drinkers, six of the eight cytology scrapings were atypical to some degree with three of the tissue specimens from these patients reported with minimal hyperchromatism. The Smoker/Drinker group (Class III) disclosed some measure of cellular atypia in eight of fifteen patients but all tissue reports were essentially normal. Class IV (Smoker-Non-Drinker) specimens were similarly equivocal. Eight of ten cytology scrapings were completely normal but three of the ten biopsies demonstrated some hyperchromatism in the basal layers. In sum, no distinct pattern of microscopic prodromata in relation to the individual smoking and drinking habits has been determined. Accordingly, the study is terminated, and an article is being written for publication.

SUPPORTED BY

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3.0059, HISTOGENESIS OF A HAMSTER FIBROHEMANGIOSARCOMA

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Simultaneous catastrophes resulted in a loss of both 2-31 and 3-31 cell lines. An attempt to re-establish a comparable cell line from the original source line (HE-44; Dr. Diamond of the Wistar Institute) was made. Cells of line HE-44 were kindly forwarded by the Wistar Institute and upon culture retained many of the properties reported for lines 2-31. However, by the fourth passage, a transformation in the cell line occurred which was noted by a lack of correlation in cell response to the inducing agent. Normal cell morphology was also remarkably different and consisted now of a large, translucent epithelial-like cell instead of the usual spindle-shaped fibroblast. Cloning was tried in vain attempt to select a cell type characteristic of cells of clone 2-31. It is possible that the difference in expression of HE-44 was related to one animal repassage as clones 2-31 and 3-31 were established from tumors induced by HE-44 cells at the Wistar Institute and the tumor bearing hamsters then forwarded. It was from these primary tumors that clonal line 2-31 was established. Since HE-44 is currently in limited supply, other methods are being tried to develop a hamster fibrohemangiosarcoma cell line.

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3.0060, PROTOCOL ON TREATMENT OF CANCERS OF THE LIPS, ORAL CAVITY AND OF 1/3 OF THE TONGUE

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OBJECTIVE and APPROACH: T2. Treatment of cancers of the lips, oral cavity and 1/3 of the tongue.

PROGRESS: (See Minerva Stomatologica 27, 1,7-14, 1978). On March 31st, 1978, 683 patients were controlled and over 228 patients treated with radiotherapy, chemotherapy and surgery. Subsequently some other patients will have to be added (the number will be specified later).

Another group of patients has been treated with cryotherapy (plus possible radiotherapy or surgery).

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3.0061, RELATIONSHIP OF BUCCAL MUCOSAL LESIONS TO THE CAUSE

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No summary has been provided to the Smithsonian Science Information Exchange.

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3.0062, MALIGNANT POTENTIAL OF ORAL LICHEN PLANUS

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The objective of this study is to obtain information on the potential for malignant transformation of oral lichen planus lesions over a 15-year period. 700 patients with histologically verified oral lichen planus are being followed. The patients are asked about past and present oral symptoms and smoking habits. The location and type of oral lichen planus lesions are registered and photographed. After the first examination the patients are seen once a year, except those with epithelial dysplasias who are seen every three months. At the follow-up examinations all changes in the lesions are recorded, photographed and, if necessary, biopsied. So far, five patients have been found with a simultaneous occurrence of lichen planus and erythroplakia. The influence of smoking on the lesions will be studied.

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3.0063, ETIOLOGY AND PREVENTION OF ORAL LEUKOPLAKIAS AND THEIR MALIGNANT TRANSFORMATION

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Oral leukoplakia is well-known as a precancerous condition. On this assumption the aim of the present study has been to analyze prospectively the aetiology and pathogenesis of oral leukoplakias as well as the aetiology and pathogenesis of carcinomas developing in such leukoplakias. In this context availability of means of early diagnosis of oral carcinoma is important. By October 1978 the study comprised 750 persons who had all had a biopsy taken at the first examination. Follow-up biopsies have been performed in case of morphological changes of the lesions. Over the years the annual follow-up for each year has covered 95.6% of the persons with only small variations from one year to another.

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3.0064, ETIOLOGICAL FACTORS IN CANCER OF UPPER RESPIRATORY AND DIGESTIVE TRACTS

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Four main groups of neoplasms (oral cavity, oropharynx, larynx and hypopharynx) are being analyzed. A comparative study is carried out with special reference to occupation, dental status, smoking and drinking habits, precancerous lesions, sex and age. This information will be compared for the four groups and for ENT Department outpatients without evidence of neoplasm.

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3.0065, INVESTIGATIONS OF ORAL CANCER AND PRECANCEROUS CONDITIONS

F.S. Mehta, Tata Inst. of Fundamental Research, Basic Dental Research Unit, *Homi Bhabha Rd., Bombay 400005, Maharashtra, India* (D-IARC-79-268)

Oral cancer is the most common form of cancer in India. It is said to be frequently preceded by white lesions termed precancerous lesions. Two studies are carried out to elucidate the natural history of these oral precancerous lesions and their association with tobacco usage. About 100,00 individuals residing in Ambegaon and Junnar Taluks of Poona districts were examined for the presence of oral precancerous lesions and tobacco usage habits. The individuals with lesions and suitably matched controls are now followed up annually. About 4,000 Bombay policemen were examined in 1959 for the presence of oral precancerous lesions and tobacco usage habits. These policemen are re-examined at five-year intervals. Three follow-ups have been completed and the fourth one is now being planned.

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3.0066, AN INVESTIGATION INTO ORAL CANCER AND ORAL PRECANCEROUS LESIONS IN INDIAN RURAL POPULATIONS IN RELATION TO TOBACCO HABITS

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Oral cancer is one of the most common forms of cancer in India. There is a strong belief that such cancer may be preceded by certain white lesions in the oral cavity, which are thus termed precancerous. It is known, mostly through hospital-based studies, that oral tobacco usage habits are associated with oral cancer and precancerous conditions. The main objectives of the present study are to (1) investigate the degree of association between tobacco usage habits, oral cancer and precancerous conditions and (2) elucidate the natural history of oral precancerous conditions from clinical and histological viewpoints. The study design is prospective in nature. In a first survey in 1967-68 conducted in five districts in different parts of India, where different tobacco usage habits prevail, 50,000 individuals were interviewed about their tobacco usage habits and examined for the presence of oral precancerous conditions. Since 1969 these individuals have been followed up annually, clinically, histologically, and cytologically, for change of habits and development of oral precancerous conditions. Follow-up surveys comprising a period of 10 years have been completed and data are now being analysed.

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3.0067, A STUDY OF THE ETIOLOGY OF CANCER OF THE HEAD AND NECK IN THE REPUBLIC OF IRELAND

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This is a retrospective case-control study of cancers of the oral cavity, nose and paranasal sinuses, pharynx and larynx. The aim of the study is to explore differences between cases and controls in relation to tobacco and alcohol consumption, social conditions, occupation, and previous medical history. Clinical data, staging of tumors, histology and treatment given will also be recorded. Patients attending St. Luke's Hospital for the treatment of skin conditions are used as controls. Controls are matched with cases by age, sex and domicile.

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3.0068, EPIDEMIOLOGICAL AND CYTOPATHOLOGICAL STUDY AMONG NATAL BETHEL-CHEWING INDIANS WITH SPECIAL REFERENCE TO SUBMUCOUS FIBROSIS

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Oral submucous fibrosis has been reported almost exclusively among Indians, especially betel/tobacco chewers. The lesion is believed to be precancerous. Qualitative and quantitative studies are being made of the Papanicolau-stained buccal smears. Epidemiological data are collected in a questionnaire at interview. Partial results of the study have been published (Proc. VI Perugia Quadrennial International Conference on Cancer. Perguia, June 1977).

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3.0069, CANCER OF THE OROPHARYNX - A CASE-CONTROL STUDY

S. Sivayoham, National Cancer Registry, Dept. of Health Services, *385 Deans Rd., Colombo 10, Sri Lanka* (D-IARC-79-497)

The data available from the Sri Lanka National Cancer Registry show that oropharyngeal neoplasms constitute 39% of all cancers in Sri Lanka. The age-adjusted rates, when compared with other cancer registries, are very high, if not the highest. For example, the age-adjusted rate for mouth cancers is 56.7 for males and 20.5 for females, many times higher than that provided by any other registry. The objective of the present epidemiological investigation is to study the association between possible risk factors, betel chewing, smoking, the consumption of alcoholic drinks, oral hygiene, socioeconomic factors, and oropharyngeal cancers in Sri Lanka. The cases will be drawn from the Cancer Institute, Maharagama, and the General Hospital, Colombo, and the control group from non-cancer inpatients of the General Hospital, Colombo.

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3.0070, LOCAL CAUSES IN THE ETIOLOGY OF HEAD AND NECK CANCER

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Local causes in the etiology of head and neck cancers (i.e., buccal mucosa, tongue, gingiva, floor of mouth, oropharynx, hypopharynx, tonsils, larynx and upper esophagus, excluding nasopharynx) are being studied. Information is sought on use of alcohol, tobacco, cleaning of teeth, kind of food taken, preferred foods, temperature at which food and drinks are taken, habit of biting the tongue or buccal mucosa and the habit of taking foreign bodies in the mouth (some drugs are retained in the mouth for a long time).

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3.0071, COMPARATIVE STUDY OF ALCOHOLISM AND CANCER OF THE HEAD AND NECK

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One hundred patients with a diagnosis of head and neck cancer were investigated carefully for a history of alcoholism in the U.S.A. Most patients with cancer of the tongue, tonsil and oropharynx were alcoholics. About one half of the patients with supraglottic carcinoma were alcoholics. In the nasopharynx and true vocal cords, there was no association with heavy drinking. The study is now being extended to Ireland since the Irish ethnic group allegedly accounts for a considerable proportion of the American drinking problem. Initial results suggest that this may be exaggerated at least as far as the cancer problem is concerned.

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3.0072, IMMUNOLOGICAL STUDIES ON CANCERS FREQUENTLY OCCURRING IN INDIA - ORAL CANCERS

S.G. Gangal, Cancer Research Inst., Biology Div., Biology Division, *Dr. Ernest Borges Marg, c/o Tata Memorial Ctr., Bombay 400012, Maharashtra, India*

OBJECTIVE: In our earlier studies we reported that oral cancer patients show cellular sensitization to autochthonous tumor extracts. The antitumor response can be maintained for 3-4 weeks in patients treated with surgery by intradermal inoculation of small doses of antigen. Experiments to increase antitumor immunity further, by inoculating patients with cauterized tumor antigen and BCG, have been undertaken.

APPROACH AND PROGRESS: Ten oral cancer patients treated with surgery received 5 mg of tumor antigen and 1 mg of BCG 2 days after operation and every 3 months thereafter. Control group was inoculated with BCG alone. Patients followed up for a year showed presence of tumor associated reactivity only in the group inoculated with BCG and tumor antigen. Marginal and temporary serum blocking activity could be demonstrated. At the end of one year, 3 patients from the experimental group remained tumor free and showed elevated antitumor immunity.

SUPPORTED BY

Dept. of Atomic Energy funds n.a.

3.0073, SMOKING AND ALCOHOL CONSUMPTION IN SOME TYPES OF CANCER (CASES AND CONTROLS)

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OBJECTIVE: 1) To prove the hypothesis linking the habit of smoking and the ingestion of alcohol with oral and laryngeal cancers. 2) To determine the risks associated with light and dark tobaccos in relation to certain types of cancer (laryngeal, oral, pulmonary, and bladder). 3) To define the relationship between various smoking habits and cancer. For example, the relationship between reverse smoking (holding the lit end of the cigarette inside the mouth) and oral cancer.

APPROACH: This study will be based on the previous findings obtained by the cancer registry in affiliation with the Social Security. Those findings indicated a disquietingly high incidence of oral and laryngeal cancers in the population studied. This high incidence was offset by low rates of lung cancer.

METHOD: The project is designed to pair off one case and two controls for each type of cancer, that is cancer of the larynx, oral cancer, lung cancer and bladder cancer. One control is matched with the case for age, sex and occupation, whereas the other control is matched for age, sex, socioeconomic class and place of residence.

PROGRESS: To date, 249 cases have been selected, but they have not been matched with controls. In February 1979, a preliminary analysis was performed, and it was determined that a minimum of 60 cases and 120 controls should be obtained for each type of cancer.

The Cancer Registry of the Instituto de Seguros Sociales of Antioquia remains active. An analysis of data for the 10 year period (1968-1967) will soon be published.

SUPPORTED BY

Inst. de Seguridad Social funds n.a.

3.0074, LONGITUDINAL STUDIES IN ORAL LEUKOPLAKIA

J. Banoczy, Semmelweis Orvostudomanyi Egyetem, Conservative Dentistry Clinic, *Mikszath Kalman ter 5, 1088 Budapest V, Hungary*

670 patients with oral leukoplakia are under continuous control over a period from 1-30 years, with a mean observation period of 9.8 years. The objectives studied are: the frequency of malignant transformation, the distribution according to age, sex, localization and smoking habits, possible etiological factors and the conditions favoring malignant transformations. In the histological material of the same leukoplakia patients the frequencies of histological dysplasia and cancer as well as the ultrastructural characteristics are studied in correlation with the clinical types of leukoplakia.

SUPPORTED BY
Ministry of Health funds n.a.

3.0075, OCCURRENCE OF EPITHELIAL DYSPLASIA IN MATERIAL OF 1000 PATIENTS WITH ORAL LICHEN PLANUS

J.J. Pindborg, Royal Dental College, Dept. of Oral Pathology, *4 Universitetsparken, DK2100 Copenhagen, Denmark*

Oral lichen planus is considered a precancerous condition by a number of authors. Therefore, lengthy follow-up studies are mandatory before a final conclusion can be reached. Of 1000 patients with oral lichen planus, those exhibiting epithelial dysplasia are followed more frequently than those without dysplasia. In some patients the oral lichen planus lesions are associated with an erythroplakia, always showing epithelial dysplasia. A few of these cases have become carcinoma. Therefore, this association needs further attention. The criteria used for the diagnosis of epithelial dysplasia are the same as used by the WHO International Reference Centre for Oral Precancerous Lesions.

SUPPORTED BY
Royal Dental College funds n.a.

3.0076, CHEMICAL CARCINOGENESIS IN CYST INDUCED IN PRIMATES

L.M. Jonck, University of Pretoria, School of Dentistry, Institute of Stomatology, *P.O. Box 1266, Pretoria 0001, Transvaal, South Africa*

The carcinogenic action of nitrosamine derivates is well known. The aim of this project is to induce neoplastic change in an experimental cyst model developed after implantation of oral epithelium in the back muscles of immunosuppressed monkeys.

In this experiment particular attention will be paid to the concentration of the carcinogen and the time lapse to affect neoplastic change in oral epithelium. An attempt will also be made to study the influence of drugs used in dentistry known to be correlated with nitrosamines.

SUPPORTED BY
South African Medical Research
Council funds n.a.

3.0077, A STUDY OF PRE-MALIGNANT AND MALIGNANT LESIONS OF THE MOUTH

C.W. van Wyk, University of Stellenbosch, Research Group in Dental Epidemiology, *Private Bag 11, c/o Prof. C.W. VanWyk, Tygerberg 7505, Cape Province, South Africa*

OBJECTIVE: To study the distribution and etiology of premalignant and malignant lesions of the mouth.

The study includes epidemiological surveys of various groups of people, with specific attention paid to habits and dietary patterns. Bona fide lesions are biopsied and examined histologically and ultrastructurally. Extensive information with regard to the pattern of oral lesions have been collected.

SUPPORTED BY
South African Medical Research
Council $20,000

TUMORS OF THE ORAL MUCOSA & CONNECTIVE TISSUES - PATHOLOGY

3.0078, DENTAL PROGRAM (HUMAN, MONKEYS)

G.H. Fletcher, University of Texas, University of Texas System Cancer Center, M.D. Anderson Hospital & Tumor Inst., Dept. of Radiotherapy, *c/o Texas Medical Ctr., Houston, Texas* 77030 (P01 CA 06294-180018)

This project is part of a broader program (CA 06294-18) whose summary states: The current and planned programs are in four areas: a) basic and applied research projects, b) clinical applications of modified and newly standardized techniques and treatment modalities, c) development and initiation of methods of data collection and analysis, and d) utilization of materials, facilities, and skills for teaching and training pre- and postgraduate students, resident physicians, and community physicians and other personnel.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Cancer Inst. funds n.a.

3.0079, STUDY OF HEAD AND NECK CANCER BY SERIAL SECTION

J.A. Kirchner, Yale University, School of Medicine, Dept. of Surgery, *333 Cedar St., New Haven, Connecticut* 06510 (R01 CA 22101-03)

III. SOFT TISSUE DISEASES

Serial section studies of surgical specimens removed for cancer by total or partial laryngectomy will be conducted with the objective of determining patterns of growth and spread within the larynx and outside this organ into adjacent structures. These studies provide the basis for determining the degree of invasion from the tumor's preoperative appearance on inspection, palpation, radiography and scanning studies. This type of knowledge allows the clinician to preserve the function of the larynx, pharynx and oral cavity when these structures must be removed for cancer in any particular case. The information is important, not only to the surgeon, but to the radiotherapist and the medical oncologist.

Cancer of the floor of the mouth, tongue, mandible and maxilla is also being studied by this technique and should provide information of value to the clinician who treats diseases and who is concerned with the preservation of function to the greatest possible degree.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$42,617

3.0080, ORAL CARCINOGENESIS, VITAMIN A AND RETINOIDS

G. Shklar, Harvard University, Boston Campus, School of Dentistry, Dept. of Oral Medicine & Oral Pathology, *188 Longwood Ave., Boston, Massachusetts* 02115 (R01 CA 23524-02)

An investigation to determine whether vitamin A, retinyl acetate, retinyl palmitate, or 13-cis-retinoic acid can retard or prevent the development of epidermoid carcinoma in two well defined oral mucous membrane tumor models - hamster buccal pouch and hamster tongue. Tumors are chemically induced by application of 9,10-dimethyl-1,2 benzanthracene (DMBA). Mineral oil is used as a vehicle for the buccal pouch applications and acetone for the tongue applications. Delayed tumor development will be evaluated grossly and microscopically.

Radioactive retinoids and radioautography will be used to determine whether the retinoids localize in oral mucosa. Chemical studies will test for aryl hydrocarbon hydroxylase.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$82,730

3.0081, STUDIES ON NORMAL AND ALTERED ORAL MUCOSA

J. Meyer, University of Illinois, Medical Center at Chicago, School of Dentistry, Dept. of Oral Pathology, *1853 W. Polk St., Chicago, Illinois* 60680 (R01 DE 02342-10)

Organ and cell culture studies using buccal mucosa from zinc-deficient rats, will be conducted. Zinc concentration and distribution will be determined by means of atomic absorption spectrophotometry and scanning electron microscopy X-ray microanalysis.

Capillaries will be visualized by means of histochemical demonstration of their alkaline phosphatase activity, permitting tracing and measurement. The size of the capillary bed in the lamina propria of regions of oral epithelium differing in width will be determined in two groups of rats aged 18 and 24 months.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$95,924

3.0082, MORPHOGENESIS OF BACTERIOPHAGE PHI-29

D.L. Anderson, University of Minnesota, Minneapolis Campus, School of Dentistry, Division of Microbiology, *6 Morrill Hall, Minneapolis, Minnesota* 55455 (R01 DE 03606-11)

We have previously described a single morphogenesis pathway for the Bacillus subtilis bacteriophage phi29 in which the 12 megadalton genome is packaged into a relatively simple prohead constructed with the aid of a recyclable core-scaffolding protein. The overall objective of the present proposal is to construct a model of phi29 that is consistent with the events that occur during assembly and to reproduce in vitro the events that lead to prohead formation and DNA-encapsidation. Specifically, we will redetermine the mass of the phi29 virion and the number of copies of each type of structural protein, and we will seek nonprotein structural components. We will study the origin, location and function of a multifunctional protein that links the ends of phi29 DNA in the virion. We will determine the stoichiometry and location of the 3-4 proteins comprising the relatively unstable prohead and the 2-3 proteins of the first stable DNA-containing intermediates. We will investigate the role of the phi29 prohead by studying DNA encapsidation in vitro, and we will attempt in vitro assembly of functional proheads from partially purified protein constituents. Finally, we will continue fine structure mapping of the cistron specifying the major head protein in an effort to correlate mutations affecting specific protein-protein interactions in head morphogenesis with map position and ultimately amino acid sequence.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $103,651

3.0083, PROTEIN KINASE INTERACTION WITH THE SALIVARY GLAND

F.J. Dowd, Creighton University, School of Dentistry, Dept. of Oral Biology, *2500 California St., Omaha, Nebraska* 68178 (R23 DE 04572-03)

This study is concerned with cyclic AMP-dependent protein kinase from the parotid gland and a description of substrates of protein kinase in membrane fractions from the parotid gland. Particular emphasis is placed on the presence of protein kinase substrates in plasma membranes and the membranes of secretory granules. Phosphorylation of the membranes in the presence of protein kinase is being tested and studied kinetically. Individual substrates will be characteized by SDS-polyacrylamide gel electrophoresis. The presence of protein kinase in various fractions of the parotid gland is also being investigated.

The possible effects of protein kinase on secretoy granule function is to be studied. This work will concentrate on the permeability characteristics of secretory granules and the effect of protein kinase on permeability.

BIBLIOGRAPHIC REFERENCES: Dowd, F.J. and Cordel, K., Protein kinase and plasma membrane-enriched fractions from rabbit parotid glands. J. Dent. Res. (abs.) 1978, in press.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

3.0084, FACTORS ASSOCIATED WITH HYPERPLASIA OF ORAL MUCOSA

R.R. Harris, University of Iowa, School of Dentistry, Dept. of Oral Pathology & Diagnosis, *Jessup Hall, Iowa City, Iowa* 52240 (R23 DE 05393-01)

Changes in the oral mucosa leading to epithelial thickening in response, for example, to tooth brushing represent functional adaptations of structure. Similar changes seen in lesions such as leukoplakia and epidermoid carcinoma are non-functional and represent derangement of normal homeostatic control mechanisms. Balanced rates of cell death and cell proliferation are necessary for homeostasis. In experimental hyperplasia, linked changes in rates of mitosis and of cellular synthesis for function have been found. Methods for assessing overall rates of epithelial metabolism have been developed by examining rates of in vitro utilization of labelling glucose, amino acids, fatty acids, uridine and thymidine by pure epithelial sheets produced from either hamster cheek pouch or ear using EDTA. Detection of a mitosis-related diurnal variation in metabolic activity and comparable rates of uptake of 14C amino acids by in vivo and in vitro techniques indicate the validity of the method.

To investigate the mechanisms by which epithelial hyperplasia is induced in oral mucosa and epidermis the in vitro assay systems for metabolism and cell proliferation will be used to 1) determine the time course and dose response curves of metabolic and proliferative changes in podophyllin, hexadecane and tetradecanoyl phorbol acetate (TPA), 2) determine the site of action of the above agents using pure epithelial sheets or intact tissue in vitro, and 3) investigate possible mechanisms of action of the agents by the use of specific pharmacologic agents.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $29,402

3.0085, CHEMISTRY AND BIOSYNTHESIS OF CONNECTIVE TISSUE

G.R. Martin, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00009-18 DB)

For summary: see 7.0005.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $54,970

3.0086, REGULATION OF COLLAGEN BIOSYNTHESIS IN NORMAL AND DISEASED TISSUES

L.M. Paglia, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of

Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00025-13 DB)

For summary: see 2.0177.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$6,423

3.0087, NETWORK DEMONSTRATION PROJECT IN HEAD AND NECK CANCER

L.W. Brady, Hahnemann Medical College & Hospital, School of Medicine, Dept. of Radiation Therapy & Nuclear Medicine, *235 N. 15th St., Philadelphia, Pennsylvania* 19102 (N01CN55255 (CONTRACT))

OBJECTIVES: Develop a regional program to demonstrate a multimodality approach to the head and neck cancer patient, including all aspects of diagnosis, treatment, and rehabilitation. Develop a maxillofacial prosthodontics program. Develop a regional head and neck cancer screening program. Develop a regional outreach educational program in all aspects of head and neck cancer for the lay public, paramedical personnel, and dental and medical professionals. Develop psychosocial support program for head and neck patients and their families. Develop a regional communications network for exchange of information in all areas of head and neck cancer.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. on Aging	funds n.a.

3.0088, CHARACTERIZATION OF CERVICAL AND SUPRACLAVICULAR LYMPH NODE ARCHITECTURE

T.C. Sist, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *3495 Bailey Ave., Buffalo, New York* 14215 (528-001-P)

This study proposes to investigate the light microscopic features of cervical and supraclavicular lymph nodes taken at autopsy from five patients free of malignant disease. At this time, LM slides have been prepared from five such cases. They have been divided into: 1. submaxillary, 2. upper cervical, 3. midcervical, 4. lower cervical and 5. supraclavicular categories. The sections were stained with hematoxylin and sosin, PAS, PAS-diastase and Alcian Blue.

Examination of the specimens from three of the five cases has yielded evidence various patterns of inflammatory change in the nodes, but no epithelial inclusions have been identified.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

3.0089, THE MECHANISMS OF EPIDERMAL TUMOR PROMOTION IN HAMSTER CHEEK POUCH

C. McGaughey, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *5901 E. 7th St., Long Beach, California* 90822 (600-002-P)

We have developed a convenient method for the quantitation of tumor promotion and progression. The method depends on the measurement of total tumor yield in two-stage tumorigenesis (overall tumor promotion) and on the proportion of total tumors which are benign hyperplastic lesions (plaques) (inversely proportional to degree of progression). We have shown that certain cell differentiating agents inhibit tumor promotion and increase the proportion of plaques thus providing confirmation for the extant hypothesis that tumor progression involves altered differentiation of cells through a series of phenotypes. The cell membrane lytic agents, trypsin, phospholipase C and triton X-100 promoted tumors primarily to the plaque stage; whereas retinyl (vitamin A) acetate and croton oil cause further progression to advanced phenotypes, including malignancy. This suggests that different mechanisms are involved in initial release from growth control and further tumor progression. The fact that large enzymes cause only early promotion suggests that the target is the plasma membrane because the enzymes probably do not penetrate into the cytoplasm. We found that 0.1M calcium ion and 10 to the minus 5th power M ionophore 23687 (a fairly specific calcium ionophore) both topically applied in DMSO also cause tumor promotion only to the plaque stage. The results for the ionophore suggest that calcium acts intracellularly. We have formulated the hypothesis that the mechanism of initial release of initiated cells from growth control is nonspecific damage to the cell membrane with consequent influx of calcium ions. Further tumor progression depends on different mechanisms. We are presently investigating the mechanism of action of calcium and of tumor progression beyond the plaque stage.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

3.0090, CYTOLOGICAL AND SEROLOGICAL STUDIES ON JAW LYMPHOMA OF MIDDLE EAST CHILDREN FOR IDENTIFICATION OF EB VIRUS

R.K. Kummoona, University of Baghdad, School of Dentistry, Dept. of Oral & Maxillofacial Surgery, *Baghdad, Iraq*

Jaw lymphoma in Middle East children is a malignant and lethal condition that differs from Burkitt's lymphoma in clinical behavior, response to treatment and possibly in its etiology. The age incidence is 2-6 years. Jaw lymphoma originates in the embryonic odontogenic tissue as a multifocal tumor; it is a highly fulminant tumor and disseminates early to the viscera. The main objectives of the present study are: 1. To investigate and identify the virus and isolate it by tissue culture. 2. To find a possible way of treatment of this highly lethal and malignant condition of the jaw.

SUPPORTED BY
(No Supporting Organization
Reported) $0

3.0091, ORO-GASTRIC CANCER AND BETEL CHEWING

J.D. Randeria, University of Durban Westville, Cancer Research Inst., *Private Bag X54001, Durban 4000, Natal, South Africa*

A cytopathological study of PAP stained buccal smears from among the betel chewing Indians with and without submucous fibrosis has been undertaken. It is found that the chewing practice started in childhood was carried over to adolescence. The females having submucous fibrosis habitually tucked the nut at one place inside the cheek and kept chewing on it. Clinically the oral submucous fibrosis was often associated with trismus which was demonstrated in the younger women who chewed only one ingredient of the betel quid, namely the betel nut. Cell counts revealed an increased exfoliation of intermediate cyanophils from lesions of oral submucous fibrosis. A further series of cases is under study.

SUPPORTED BY
(No Supporting Organization
Reported) funds n.a.

3.0092, ORAL FOCAL EPITHELIAL HYPERPLASIA (ABBREV)

F. Praetorius, Kobenhavns Tandlaegehojskole, Dept. of Oral Pathology, *Universitetsparken 4, DK2100 Copenhagen OE, Denmark* (D-IARC-79-135)

Oral focal epithelial hyperplasia is widespread among Eskimos and Amerindians, but rare among Caucasians (Europides). In Greenlanders there seems to be a direct relationship between the prevalences found and the degree of mixture of the population with Caucasians. This may be due to an influence of a genetic factor, and serological studies are, therefore, performed. Histology and electron microscopy seem to indicate a viral etiology of the disease; the size and morphology of the virus-like particles correspond to what has been described in verruca, condylomata, and in oral papillomatosis in dogs and rabbits. Pilot studies with immunofluorescence technique have shown that the patients with focal epithelial hyperplasia produce antibodies against an antigen in the affected cells. It is likely that the disease is contagious. Epidemiological studies have been performed on 3,500 persons in Greenland and on population groups of Greenlanders and Danes in Denmark. Follow-up studies are undertaken in Greenland. Electronic data analysis of the collected material is performed in collaboration with J.E. Bearman. Blood group type studies are done on saliva samples from the same persons and are performed in collaboration with Dr. H. Guertler, Copenhagen. Family studies are carried out in collaboration with Dr. R. Gessain, Paris, who is in possession of records of the entire Eskimo population of the east coast of Greenland, dating back to about 1820. Biopsies from Greenland are studied histologically and ultrastructurally; immunofluorescence studies are also carried out. The electron microscopic studies are performed in collaboration with Dr. O.Fejerskov, Arhus, Denmark. Tissue culture studies are also performed.

SUPPORTED BY
(No Supporting Organization
Reported) funds n.a.

3.0093, CORRELATION BETWEEN EPITHELIAL DYSPLASIA AND PRESENCE OF CANDIDA IN ORAL LEUKOPLAKIAS

J.J. Pindborg, Royal Dental College, Dept. of Oral Pathology, *4 Universitetsparken, DK2100 Copenhagen, Denmark*

As it is known that a Candida infection in most cases is associated with a nodular (speckled) leukoplakia, characterized by epithelial dysplasia, carcinoma in situ or squamous cell carcinoma, it is felt necessary to study this association in depth in order to ascertain whether the dysplasia may be reversible, especially since mutilating surgeries have been performed in patients with Candida-infected leukoplakias exhibiting epithelial dysplasia. In material of 700 patients with oral leukoplakias, which are followed regularly, the Candida-infected leukoplakias are given an antimycotic treatment.

When the lesions have disappeared or become homogeneous a new biopsy is taken. A pilot survey has demonstrated that some of the dysplasias are reversible.

SUPPORTED BY
Royal Dental College funds n.a.

TUMORS OF THE ORAL MUCOSA & CONNECTIVE TISSUES

- DIAGNOSIS & TREATMENT

3.0094, ADJUVANT CHEMOTHERAPY IN HEAD AND NECK CARCINOMA

S.K. Carter, Northern California Cancer Program Inc., *770 Welch Rd., Suite 190, Palo Alto, California* 94304 (N01CM87154 (CONTRACT))

Test the effects of high dose chemotherapy before surgery on Head and Neck Squamous Carcinoma.

SUPPORTED BY
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst. funds n.a.

3.0095, PI-MESON RADIOTHERAPY OF ORAL CAVITY CARCINOMA (HUMAN)

M.M. Kligerman, University of New Mexico, School of Medicine, Dept. of Radiology, *University Hill N.E., Albuquerque, New Mexico* 87131 (P01 CA 16127-060026)

This project is part of a broader program (CA 16127-06) whose summary states: The primary objective of this program is to conduct the necessary physical, biological and clinical studies to evaluate the efficacy, potential benefit and role of negative pi mesons (pions) in management of all types and stages of solid tumors not well managed by current methods or combinations thereof. The University of New Mexico Cancer Research and Treatment Center and the Los Alamos Scientific Laboratory have been engaged since 1972 in a joint research effort to test the radiotherapeutic potential of pions produced by the 800 MeV proton linear accelerator at Los Alamos. This accelerator is the only one in the world presently capable of producing pions at sufficient intensity for medical testing, and institutions throughout the nation are sending appropriate patients to this facility for pion radiotherapy. These studies have been conducted in the past under two grants (CA-14052 for preclinical studies and CA-16127 for clinical studies); the two grants are being combined in this application. Randomized Phase III clinical trials of pion radiotherapy for 13 anatomic sites are expected to be activated by the start of the three-year period proposed in this application. Progress to date in the clinical, biological, and physical studies, as well as research plans for the proposed three-year period are described in the text of this application for each of the four components: clinical investigations, biology, physics, and core.

SUPPORTED BY
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst. funds n.a.

3.0096, EVALUATION OF REHABILITATION OF OROPHARYNGEAL CANCER

J.A. Logemann, Northwestern University, Chicago Campus, School of Medicine, Dept. of Otolaryngology & Maxillofacial Surgery, *303 E. Chicago Ave., Chicago, Illinois* 60611 (R18 CA 18901-05)

This study is designed to: 1) evaluate the effects of ablation surgery of the oral cavity and oropharynx and associated reconstructive surgery on the psychological, communicative, and nutritional rehabilitation of patients with cancers of these areas; 2) assess the effectiveness of speech and swallowing rehabilitation in improving communication and deglutition; and 3) define the most effective rehabilitation techniques used to increase the patient's speech and swallowing function. Ninety patients with oral cancer requiring surgical treatment will be studied at five points in their protocol: 1) before initiation of any treatment; 2) after radiation, if given (pre-or post-op); 3) after ablative surgery; 4) after the final surgical procedure to close any remaining fistulas or to reconstruct oral structures and before initiation of any rehabilitative intervention; 5) six months after initiation of oral feeding and speech and swallowing therapy. On each of these testing dates, each patient will complete a thorough examination protocol including detailed studies of: 1) oral, pharyngeal, and esophageal function during deglutition; 2) oral and pharyngeal function during speech; 3) the source (neurologic) and extent of pain he experiences, if any; 4) his pattern and method of social communication; and 5) his psychosocial status. These evaluations will generate a profile of the patient's modal functioning at each point in his recovery. With the patient acting as his own control, the pre- and post-treatment profiles will be compared to provide an objective picture of the effects of the ablative surgery, surgical reconstruction, and speech and swallowing therapy on the patient's typical psychosocial and physiologic functioning.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$77,357

3.0097, REHABILITATION OF THE HEAD AND NECK CANCER PATIENT

M.C. Robson, University of Chicago, School of Medicine, Dept. of Surgery, *5801 S. Ellis Ave., Chicago, Illinois* 60637 (R18 CA 20396-02)

A multidisciplinary team approach for treatment and rapid rehabilitation of head and neck cancer patients is being evaluated. Rehabilitation begins as soon as the diagnosis is confirmed, rather than being delayed until treatment has been completed. New surgical and maxillofacial prosthodontic procedures are being evaluated to reconstruct head and neck defects using microvascular anastomoses for the transfer of soft and osseous tissue and alloplastic prostheses implanted by magnets or staples. This will allow the physical reconstruction time to be dramatically shortened and total psychosocial, dental, and speech rehabilitation to be completed more effectively.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$66,276

3.0098, ACYL COENZYME A HYDROLASE(S) OF RAT SALIVARY GLANDS

T.E. Knauer, Virginia Commonwealth University, Medical College of Virginia, Dept. of Medicine, *1200 E. Broad St., Richmond, Virginia* 23298 (R23 DE 05000-02)

This project concerns the role of palmitoyl coenzyme A hydrolase (EC 3.1.2.2) and acyl CoA hydrolases in the regulation of lipid metabolism. The hydrolase activities of rat submaxillary gland, brain, and other tissues will be measured under a variety of physiological, pharmacological, hormonal, and nutritional states of the rat to determine if this enzyme contributes to the modulation of intracellular concentrations of long-chain acyl CoA thioesters. Purification and characterization of the hydrolases from submaxillary gland and brain will be attempted. Mechanisms of regulation of these enzymes in vitro (i.e., product or substrate inhibition, allosterism, etc.) will be investigated and attempts made to correlate these findings with the physiology of the animal. In particular, the relationship between the secretory activity, energy production via lipid metabolism, and the activity of palmitoyl CoA hydrolase will be investigated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

3.0099, TECHNIQUES FOR EARLY DETECTION OF ORAL CARCINOMA

A. Mashberg, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Tremont Ave. & S. Centre St., East Orange, New Jersey* 07019 (Y01DE40014 (CONTRACT))

OBJECTIVES AND WORK SCOPE: A study to develop and evaluate clinical criteria for the early detection of oral carcinoma and to evaluate toluidine blue and a DNA-acridine binding test as techniques for detection of clinically inapparent carcinoma and as techniques for identifying patients with precancerous field alterations of the oral mucosa.

SALIENT RESULTS TO DATE: The study to date has resulted in identifying a group of 130 patients who had suspicious oral lesions. In this group 62 asymptomatic invasive oral carcinomas have been diagnosed by histopathologic criteria. Thirteen carcinomas in situ have been identified, nine lesions were dysplastic in nature (not yet carcinoma) and 85 lesions were benign. From this and a previous group of patients, clinical criteria for size, location, and appearance have been developed which have a high reliability factor (low false negative rate) for identifying early asymptomatic oral carcinomas.

Studies have also been initiated to evaluate the potential value of toluidine blue staining as a method of enhancing the detection and clinical diagnosis of early asymptomatic carcinomas of the oral cavity. Presently the false negative rate is less than 10%.

Studies of secondary primary carcinomas show that 23% of the patients with asymptomatic oral carcinomas had a non-oral primary lesion in the upper aerodigestive tract. Only 9% of patients with benign oral lesions had a malignancy in the upper aerodigestive tract. When restrospective, concurrent, and prospective development of carcinomas in all locations, including the oral cavity, was examined in the same group of patients the incidence of secondary primary cancer was 43%. This is over twice the number previously reported in the literature.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,

III. SOFT TISSUE DISEASES

National Inst. of Dental Research	$77,040

3.0100, SECSG 79 HN 356 FOR STAGE III AND IV EPIDERMOID CARCINOMA OF ORAL CAVITY OF HYPOPHARYNX AND LARYNX

S.D. Williams, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *1481 W. 10th St., Indianapolis, Indiana* 46202 (583-004-I)

Patients with newly diagnosed Stage III or Stage IV epidermoid carcinoma of the oral cavity, hypopharynx or larynx will be randomized to receive or not to receive pre-operative chemotherapy. Patients with T4 N3 lesions are considered too advanced for this protocol and are not eligible. Chemotherapy will consist of methotrexate 70 mg/M2 I.V. push every six hours for four doses followed by leucovorin factor rescue consisting of leucovorin factor, 6 mg. intravenously every six hours for nine doses. Bleomycin will be given in a dose of 30 mg intraveneously every seven days for six doses. Cis-platinum 2 mg per kg will be given by I.V. drip on day three, and repeated on day 24. If no toxicity occurrs the methotrexate dose will be escalated to 140 mg/M2 and given on day 21, followed again by folinic acid rescue. Patients will then be evaluated for surgery. Those demonstrating metastatic disease or unresectable lesions will be taken off study. Following surgery, patients will receive radiation therapy consisting of 5,500 to 6,000 rad over five to seven weeks. Patients randomized to receive no chemotherapy will be subject to identical surgical techniques and radiation therapy. The two groups will be compared for disease-free survival, toxicity and complications. The rate of response to the combination chemotherapy regimen prior to surgery will be evaluated.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

3.0101, DEVELOPMENT OF AN ORAL LEUKOPLAKIA PRONENESS PROFILE

O.R. Koski, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *1030 Jefferson Ave., Memphis, Tennessee* 38104 (614-001-P)

The protocol for this pilot project calls for the study of 20 human subjects, ten with oral leukoplakia and ten control, including: physical examination; biopsy and cytology specimens; social and medical history; tobacco, alcohol, and drug experience; triceps skin fold measurement; a dietary questionnaire; immunologic studies on circulating lymphocytes; and determination of levels of several routine and special metabolites and nutrients in blood and urine. At present we have studied seven experimental and three control subjects all of whom were patients at the Veterans Administration Medical Center, Memphis, Tennesseee. All phases of data gathering have been completed except for determinations of blood and urine metabolites and nutrients for which serum, plasma, and urine have been frozen and stored. These fluids are to be analyzed after these specimens have been collected from all subjects, for reasons of expediency and economy. Also, lymphocyte studies have been performed on only four experimental and three control subjects because of early technical difficulties in processing. A superficial analysis of data gathered to date, in the absence of forthcoming determinations on blood and urine specimens, indicates that leukoplakia patients 1) are almost invariably habitual users of tobacco and alcohol; 2) tend to subsist on a sub-optimal diet; and 3) often have a history of borderline hyperchromic-macrocytic anemia. The project should be completed by December 31, 1979. Future allied studies will depend on project results.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

3.0102, CLINICAL TRIALS ON DIFFERENT MODES OF TREATMENTS OF ORAL CANCER, AND CANCER OF THE ESOPHAGUS AND BREAST

A.K. Mukherjee, Medical College Hospitals, Dept. of Radiotherapy & Nuclear Medicine, *Chevayoor Kerala, Calcutta 700073, West Bengal, India*

OBJECTIVES: 1) Clinical trials on treatment of oral cancers of different types by the following three modes of combination treatments: a) chemotherapy in suitable combinations followed by radiotherapy; b) chemotherapy in suitable combinations followed by surgery; and c) chemotherapy in suitable combinations followed by both surgery and radiotherapy. 2) Treatment of cancer of the esophagus with chemotherapy in different combinations followed by radiotherapy. 3) Treatment of cancer of the breast and differential variations of standard modes of treatment at different stages of the disease.

APPROACH: For 1, 2 and 3, different combinations of treatment are given to the patients and their clinical results are being followed up.

PROGRESS: The clinical results are being studied and more data are being collected.

SUPPORTED BY

(No Supporting Organization Reported)	funds n.a.

3.0103, PROGNOSTIC FEATURES IN THE HISTOPATHOLOGY OF ORAL SQUAMOUS CELL CARCINOMA

N.W. Johnson, University of London, London Hospital Medical College, Dept. of Oral Pathology, *Turner St., London E1 2AD, England, United Kingdom*

This study is designed to seek correlations between clinical and histopathological features and the prognosis of patients with squamous carcinoma of the oral mucous membrane. A wide range of histological features is scored from sections of the original diagnostic biopsy on semi-quantitative basis. These include features of both the epithelium and the tumor stroma.

Data are analyzed using the statistical package for the social sciences with corrections for age employing both the Peto and Peto method and the Cox method.

Preliminary data indicate that many variables traditionally regarded as of importance, such as mitotic activity, do not by themselves strongly influence survival. Among the epithelial features, the diffuseness of the infiltration pattern is the strongest unfavorable prognostic sign. Amongst connective tissue features, the density of immune inflammatory infiltrate is positively correlated with survival.

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3.0104, AN INTERVENTION STUDY OF ORAL CANCER AND PRECANCEROUS LESIONS IN RELATION TO TOBACCO USE IN RURAL INDIAN POPULATIONS

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Through follow-up studies for the last ten years it has been established that tobacco usage in the various forms practiced in different parts of India is definitely associated with oral cancer and precancerous lesions. The incidence of precancerous lesions among those who do not use tobacco in any way was almost zero, whereas the incidence among those who do ranged from 1 to 35 per 1,000 per year, depending upon the form of usage. The next step is to determine whether the association between oral cancer and precancerous lesions and tobacco usage is direct by demonstrating a reduction in the incidence of precancerous lesions when the tobacco usage is discontinued. A sample of 12,000 individuals using tobacco has been examined and interviewed in each of the three rural areas under study. A concentrated program of education, motivation and guidance has been prepared to persuade these villagers to give up tobacco. The villagers are shown a documentary film, especially made for this purpose, in the vicinity of their homes, in the most suitable format formulated after conducting impact studies of the film in each of the three areas. The message is also communicated personally to each of the examined individuals. In addition, the population is subjected to visual, audio and other media support. These individuals are reexamined annually to assess changes in tobacco usage habits, development of new oral precancerous lesions and changes in previously diagnosed lesions.

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3.0105, MODIFYING EFFECT OF DIET ON UPPER ALIMENTARY TRACT CANCER IN PERSONS WHO CHEW AND SMOKE TOBACCO

P.N. Notani, Cancer Research Inst., Epidemiology Div., *Dr. Ernest Borges Marg, c/o Tata Memorial Ctr., Bombay 400012, Maharashtra, India* (D-IARC-79-270)

Tobacco chewing and smoking habits carry a high risk for oral cancers, yet not all those who chew or smoke heavily get the disease. This indicates a role for other factors which may have a modifying effect on these risks. Preliminary analysis of existing records indicated a reduction in oral cancer risk in persons with tobacco chewing and smoking habits whose diet included eggs, meat or fish (Ind. J. Cancer, 13, 1976). It is intended to devise methods for collection of dietary information, confirm preliminary observations on oral cancer by a case-control study and extend the study to cover pharyngeal and esophageal cancers.

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TUMORS OF THE ORAL MUCOSA & CONNECTIVE TISSUES - PREVENTION

3.0106, CHARACTERIZATION OF ORAL MUCOSA AND SKIN BASAL LAMINA

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The following are the broad-based objectives of the proposed investigation: 1. To isolate stratified squamous epithelial basal lamina (SSE-BL) from oral mucosa and skin and to subsequently purify its individual components. This will be accomplished by solubilizing the lamina in a variety of denaturing and reducing agents and then fractionating the soluble components by a combination of gel filtration, ion exchange and affinity chromatography. 2. To elucidate the major chemical and physicochemical characteristics of the purified proteins. Chemical characteristics to be determined are amino acid composition by automated analysis, carbohydrate composition by gas-liquid chromatography and terminal amino acid analysis by specific chemical reaction. 3. To immunologically characterize BL from bovine skin and oral mucosa and human and rat skin by immunohistochemical, immunocytochemical, immunochemical and immunoelectrophoretic techniques. Immunological identity and cross-reaction with basal laminae from homologous and heterologous tissues and species will be determined. Ultrastructural localization of the antigenic determinants of BL will be established using immuno-electron microscopy with peroxidase conjugated antibody. 4. To study BL changes in a group of diseases which manifest their pathology in the mucosa of the oral cavity, including: squamous cell carcinoma, bullous and benign mucous membrane pemphigoid and adenoid cystic carcinoma. 5. To study BL synthesis during wound healing and during embryonic development utilizing anti-rat and anti-human BMZ antibodies for fluorescent antibody and immuno-electron microscopic evaluation.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $87,052

TUMORS & OTHER DISEASES OF SALVIARY GLANDS - EPIDEMIOLOGY

3.0107, GENETIC AND EPIDEMIOLOGICAL STUDY OF SALIVARY PROTEINS

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Human parotid saliva contains many acidic proteins which are genetically determined. Studies have indicated that certain acidic salivary proteins absorb onto enamel surfaces, and that these proteins could be involved in the organization and development of the plaque matrix. The purpose of this study was to investigate the possible influence of salivary phenotype on individual proclivity to develop dental plaque, periodontal disease and/or caries. Each subject was clinically examined to determine their DMFS score, periodontal and dental plaque indices. A parotid saliva sample was collected for phenotyping. Pr and Db salivary phenotypes were analyzed with data obtained from 63 Caucasian subjects by one-way analysis of variance. Subjects that were phenotypically Db plus had a significantly (P less than 0.05) higher plaque index and higher periodontal index than Db-individuals. Thus far correlations were not discerned between Pr phenotypes and clinical observations. Chi-square analysis showed a disproportionate number of individuals with both Pr 1-2' and Db-phenotypes. There are indications that Caucasian individuals with the Db plus phenotype are more prone to developing dental plaque with concurrent periodontal disease.

BIBLIOGRAPHIC REFERENCES: Friedman, R.D. and Karn, R.C. (1977) Immunological Relationship and a Genetic Interpretation of Major and Minor Acidic Proteins in Human Parotid Saliva. Biochem. Gen. 15, 549-561. Karn, R.C., Friedman, R.D., Laughner, W.J., Merritt, A.D. and West, L.J. (1977) Purification and Partial Characterization of Human Salivary Protein-Rich Proteins. FASEB Meeting, Chicago, Ill.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

3.0108, MECHANISMS OF SALIVARY GLAND DEVELOPMENT

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The object of this proposal is the study of differentiation of secretory cell types in rodent salivary glands. With specific antisera and enzyme assays, it proposes to measure the rates of synthesis, turnover and secretion of cell type specific markers during the appearance or disappearance of the terminal tubule, acinar and granular duct cells. These studies will provide a precise biochemical description of the process of differentiation in these cells. The proposal also includes a study of the stability cf the differentiated phenotype of salivary gland secretory cells in cell culture. Preliminary studies indicate that parotid acinar cells attach and synthesize alpha-amylase for at least two weeks in culture. Using this approach, a plan is outlined which explores the cellular origins of the secretory cells and the factors which influence their appearance or disappearance.

SUPPORTED BY

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3.0109, SALIVARY SECRETION-ROLE OF CALCIUM

E.L. Watson, University of Washington, School of Medicine, Dept. of Pharmacology, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (R01 DE 05249-01)

The main objective of the proposed research is to further elucidate the role of calcium in cholinergic stimulation of amylase from salivary glands. Accumulated evidence suggests that secretion is dependent on the level of cytoplasmic calcium made available from the extracellular fluid and/or from intracellular storage depots; increases in cytoplasmic calcium initiate the secretory process. The proposed studies will be aimed at examining the contribution of extracellular calcium and calcium derived from internal stores to the release of amylase from mouse parotid glands. The effects of the cholinergic agonist, carbachol, on 45Ca influx and efflux from parotid fragments will be determined and correlated with amylase release. The adrenergic agonist, isoproterenol, will be examined since this agent also stimulates amylase release but does not appear to require extracellulr calcium. Adrenergic agonists utilize cyclic-AMP as an 'intracellular messenger'. During cholinergic stimulation of amylase release there is an increase in cyclic-GMP (c-GMP) levels in salivary tissue. The relationship between changes in cytoplasmic calcium levels and in the levels of c-GMP brought about by cholinergic as well as adrenergic stimulation will be evaluated by use of inhibitors of calcium influx and by the calcium ionophore, A23187. 45Ca fluxes across isolated secretory granules will be examined to determine the possible contribution of the secretory granule as a calcium storage depot. The purity of such granules will be established via biochemical and electron microscopic studies.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$70,099

3.0110, GENETIC AND EPIDEMIOLOGICAL STUDY OF SALIVARY PROTEINS

R.D. Friedman, University of Pennsylvania, School of Dental Medicine, Dept. of Oral Medicine, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (R01 DE 05528-01)

The principal aim of this proposal is to determine those specific heritable salivary proteins that influence human susceptibility to caries and/or periodontal disease. Sample of parotid saliva will be collected from 300 donors and electrophoretically phenotyped for the salivary genetic markers, Pa, Pb, Db, Pr, Gl, Ps and Pm. Data from these same subjects will include a DMFS Index, Peridontal Index, Plaque Index, Age, Sex, Race, Oral Hygiene Index, Smoking Habit and a Nutritional Record. The relationship between genetic factors and clinical or epidemiological scores will be investigated by analysis or covariance (ANCOVA). Significant effects for genetic factors or combinations of genetic factors will be measured by either the raising or lowing or clinical indices. Salivary phenotypes or combinations of phenotypes that show a significant increases in clinical disease indices will be considered predisposed to dental disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$19,747

3.0111, CONTROL MECHANISMS IN SALIVARY GLAND DEVELOPMENT

J.H. Sheetz, University of Alabama in Birmingham, School of Medicine, Dept. of Anatomy, *1919 7th Ave. S., Birmingham, Alabama* 35233 (R23 DE 05142-01)

Since salivary glands and their secretions play an essential role in maintaining the oral environment, information on the development and differentiation of the secretory units may lead to a better understanding of the functional aspects of these organs in health and disease. Normal activity of salivary glands is controlled by neural stimulation and recent studies on rodents suggest that experimental stimulation with synthetic catecholamines, especially isoproteren l (ISP), leads to alteration of salivary gland structure and function. This study is proposed to determine the role of the Beta-adrenergic activity, elicited by ISP, on the morphological development and biochemical differentiation of the major salivary glands, and therefore, demonstrate a neural control mechanism in their development. ISP treatment of postnatal rats will begin prior to the period in which the salivary glands show the greatest amount of development. The effects of the Beta-adrenergic antagonist propranolol will also be studied after treatments comparable to those of ISP. Morphological development of the parotid, submandibular, and sublingual will be determined by electron microscopic studies and biochemical differentiation will be determined by monitoring changes in protein patterns in the glands by acrylamide gel electrophoresis. It is anticipated that excessive Beta-adrenergic stimulation by ISP will induce exaggerated changes in the glands representative of discrete cellular changes which progress more slowly in normal development. Inhibition of normal development by propranolol will strengthen the supposition that Beta-adrenergic stimulation plays an important role in controlling development of the major salivary glands.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$23,948

3.0112, STUDIES ON THE ORAL PHYSIOLOGICAL STATUS OF MAN DURING AGING

B.J. Baum, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. on Aging, Intermediary Metabolism Section, *Baltimore, Maryland* 21224 (Z01 AG 00049-01 LMA)

There has been little systematic investigation of tissues within the aging oral cavity. It is the purpose of this project to assess the oral physiologic status of participants in the Baltimore Longitudinal Study and thus provide baseline information which is, at present, essentially lacking. The study has two major objectives: (1) to define subjects acccording to their dental and oral health; to examine biological factors which are likely to influence oral health. The latter include studies of salivary gland function (saliva output: quantity and constituents) and studies on dental plaque (bacterial population and plaque fluid components).

BIBLIOGRAPHIC REFERENCES: Baum, B.J.: Salivary glands and saliva: recent advances in understanddng their function and role in oral health. The New Dentist 9: 21-26, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. on Aging	funds n.a.

3.0113, TRI-COUNTY STUDY OF CANCER OF THE MOUTH, ESOPHAGUS, LARYNX, STOMACH, COLON AND RECTUM

S. Graham, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *3495 Bailey Ave., Buffalo, New York* 14215 (528-001-P)

In this study, subjects are interviewed with regard to dietary habits, smoking, occupation, medical and dental history. We have interviewed 76 patients from the Veterans Administration Hospital since 1975. To date, we have not obtained enough data for definitive analysis; therefore, we have not reported any results or conclusions. However, preliminary analysis of 100 case/spouse and 100 control/spouse pairs to determine extent of agreement with regard to the subjects' dietary habits is under way. We plan to continue interviewing for approximately 2 more years.

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3.0114, DEVELOPMENTAL BIOLOGY OF RAT PAROTID GLAND

R.S. Redman, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *1055 Clermont St., Denver, Colorado* 80210 (554-002-P)

Support for this project was terminated August 26, 1978, because the principal investigator was transferred to the Washington, D.C., Veterans Administration Medical Center. However, a large amount of material was prepared for analysis prior to the transfer, and is being analyzed and prepared for publication at the new station. It is anticipated that a final report will not be submitted until the next anniversary of the initiation of the project.

In collaboration with Dr. David O. Quissell, University of Colorado Medical School, a model was developed for studying the regulation of secretion in the rat submandibular gland. Glands were subjected to enzymatic digestion, followed by gentle mechanical disruption, sieving and differential centrifugation. This provided a cell fraction greatly enriched with acinar-intercalated duct complexes that were in excellent condition, as shown by electron microscopy and biochemical assays that test for cell viability. These intact but unfettered primary secretory complexes reacted to a variety of ions and secretagogues in a manner that appears to be superior to any previously reported system utilizing dissociated salivary gland components.

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TUMORS & OTHER DISEASES OF SALIVARY GLANDS - ETIOLOGY

3.0115, NCI HISTOCOMPATIBILITY TESTING CENTER

A.H. Johnson, Duke University, School of Medicine, Dept. of Microbiology & Immunology, *Box 3711, Durham, North Carolina* 27710 (N01CB53890 (CONTRACT))

HL-A phenotyping of approximately 2,500 samples. Maintenance of panel of cells well defined for HL-A antigens. Assessment of serums for antibodies to HL-A and other antigens by the lymphocyte cytotoxicity assay. Mixed lymphocyte cultures: Perform approximately 400 MLC reactions between lymphocytes from blood samples provided by the P.O. and a panel of donors accessible to the contractor, who have defined allelles at the MLC locus; and Perform approximately 100 MLC reactions between pairs of blood samples provided by the P.O.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

3.0116, CHEMICAL RADIOPROTECTION BY WR-2721 OF PAROTID GLANDS

M. Sodicoff, Temple University, School of Medicine, Dept. of Anatomy, *3322 Broad St., Philadelphia, Pennsylvania* 19122 (R01 DE 03666-05)

Past work in our laboratory established the x-ray dose-response characteristics of the rat parotid gland over the dose range of 0.4-6.kR. These baseline studies utilized both morphologic and physiologic criteria; electron microscopy established the morphologic response and size and residual amylase content the physiologic condition of the gland following irradiation.

Our current work is involved with attempting to protect the parotid from the ravages of high doses of x-ray utilizing a new experimental chemoradioprotector WR-2721 (S-2 (3-aminopropylamino) ethyl phosphorothioic acid). To date the compound has shown itself to be highly effective in protecting the parotid against loss of size and function during the first week after irradiation. We are attempting to show that the drug will be effective long after irradiation and hope to elucidate the mechanism of the protection. We also anticipate studies which will combine the selective protective effects of WR-2721 on normal tissues with the equally selective sensitizing effects on tumors of compounds such as metronidazole in an attempt to increase the therapeutic ratio for radiotherapy patients who frequently suffer from xerostomia (dry mouth).

BIBLIOGRAPHIC REFERENCES: M. Sodicoff, N.E. Pratt, P. Trepper, M.M. Sholley and S. Hoffenberg, Effects of X-Irradiation and the Resultant Inanition on Amylase Content of the Rat Parotid Gland. Arch. Oral Biol. 22:261-267, 1977.

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U.S. Dept. of Health & Human
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National Inst. of Health,
National Inst. of Dental
Research $0

3.0117, CELLULAR PHARMACOLOGY OF SALIVARY SECRETION

J.W. Putney, Wayne State University, School of Medicine, Dept. of Pharmacol, *1014 Rivard, Detroit, Michigan* 48207 (R01 DE 04067-05)

The proposed project will continue to deal with the cellular pharmacology of salivary secretion with an in vitro parotid gland preparation. An attempt will be made to delineate the mechanisms by which the receptors regulate second messengers such as Ca and cyclic nucleotides. The receptor mechanism include cholinergic, peptide, alpha-adrenergic and Beta-adrenergic. Additionally, the mechanisms by which these processes regulate exocytosis, and membrane permeability to other electrolytes will be sought. A combination of biophysical, biochemical and morphological approaches will be used. Biophysical studies will include flux measurements and component analysis for Ca, Na, K and Cl, the biochemical studies will examine the role of cyclic nucleotides, phosholipids, and surface receptors and the morphological approach will utilize correlated ultrastructural studies with the electron microscope. Ultimately, unifying hypotheses may be developed describing the cellular and molecular mechanisms by which autonomic agents affect cell functions and describing the basic mechanisms of salivary secretion. Such information may prove useful in the future as the role of saliva in dental health becomes more apparent.

6

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3.0118, CONTROL OF PERIODONTAL DISEASES - DESIGN OF NEW AGENTS

R.A. Coburn, State University of New York, Health Science Center at Buffalo, School of Pharmacy, Dept. of Medicinal Chemistry, *3435 Main St., Buffalo, New York* 14214 (R01 DE 04744-03)

The objective of this research is the development of new chemotherapeutic agents for the control of human oral plaque and periodontal diseases. This objective will be accomplished by the design and selection of agents from structural classes of currently known, clinically effective agents. Attention in this project is focused upon those agents which may act by inhibition of microbial growth. Agents with properties resulting in their retention in the oral cavity are favored.

Two classes which have been selected for structural development are the bis-biguanides and the salicylanilides. Previous studies of bis-biguanides and preliminary work indicates that bis-biquanide agents superior to chlorhexidine or alexidine may be found among aliphatic derivatives with compact but highly lipophilic terminal groups. Bis-biguanides with benzylic and cyclic aliphatic terminal groups will be synthesized and evaluated for in vitro antimicrobial activity as well as antiplaque activity via a newly developed in vitro tooth slab assay. The microorganisms involved in these studies include Actinomyces viscosus, Actinomyces naeslandii, Streptococcus mutans, Streptococcus sanquis, Actinomyces Israelii, and Gram negative rods isolated from patients with juvenile periodontitis. Repetitive cycles of syntheses and evaluation are planned in order to optimize activity. These bis-biguanides will incorporate both conventional bridge moieties and more rigid bridges designed to increase binding of the agents to salivary proteins.

The design and syntheses of salicylanilides and salicylanilide analogs will be undertaken to produce agents in this class of antibacterials with antiplaque properties superior to those of tribromsalan, a clinically effective antiplaque agent. A series of nonhalogenated n-alkyl salicylanilides and salicylamides of amino-heterocycles will be prepared and evaluated for in vitro antimicrobial and antiplaque properties. Agents, in both classes, with optimal in vitro activities will be further evaluated in vivo for control of the development of gingivitis and periodontitis in animals.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $82,763

3.0119, NEUROEFFECTOR TRANSMISSION IN A SIMPLE SALIVARY GLAND

D.M. Senseman, University of Pennsylvania, Monell Chemical Senses Center, *203 Logan Hall, Philadelphia, Pennsylvania* 19104 (R01 DE 05271-01)

The objective of the proposed research is to develop and study a new salivary gland and neuroeffector preparation from the basomatophoran snail Helisoma trivolvis. The relative simplicity of the system's morphology and innervation in conjunction with its amenability for intracellular microelectrode analysis suggests that it will provide a useful model for electrophysiological and ultrastructural analysis of the cellular processes underlying stimulation-secretion coupling. The initial step of our analysis will be to reassess and extend the current evidence favoring the existance of a monosynaptic connection between the salivary effector neuron and acinar gland cells. If the connection is monosynaptic, we will attempt to identify the neurotransmitter released by the effector neuron using pharmacological, neurochemical and ultrastructural criteria. The puntative transmitter substance(s) for this synapse will then be used to study the ionic bases of excitation-secretion coupling in acinar gland cells.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $28,130

3.0120, ROLE OF THE REGIONAL LYMPH NODE IN ORAL NEOPLASIA

R.W. McWilliams, University of Maryland, Baltimore Professional Schools, School of Dentistry, Dept. of Oral Diagnosis, *66 W. Baltimore St., Baltimore, Maryland* 21201 (R23 DE 04774-02)

The purpose of this study is to examine and compare the relative in vitro cell-mediated reactivity of lymphocytes from regional lymph nodes, distant lymph nodes, spleen and peripheral blood of rats bearing spontaneous (chemically induced) as well as transplantable syngeneic oral tumors.

Highly purified lymphocytes and tumor cells are being harvested and the degree of cell-mediated reactivity monitored at various stages of tumor progression by the use of a microcytotoxicity assay.

In addition to providing a new study model, this analysis may further our knowledge of the importance of the regional lymph node in the immune response to oral neoplasia. This could have direct importance with respect to clinical chemotherapeutic and surgical treatment of oral cancer.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $13,870

3.0121, ULTRASTRUCTURE AND CYTOCHEMISTRY OF SECRETORY CELLS

A.R. Hand, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Experimental Morphology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00028-12 LBS)

Basic mechanisms of the secretory process are studied in cells of the rat pancreas, salivary and lacrimal glands. Techniques utilized include light and electron microscopy, cytochemistry, radioautography, and biochemical determination of enzyme and cyclic nucleotide levels. Major areas of investigation are: (1) the role of the Golgi apparatus and GERL in secretory granule formation; (2) the structure and function of GERL and cyclic nucleotide levels in secretory cells of the beige mouse, a homologue of the human Chediak-Higashi syndrome; (3) the role of lysosomes in the intracellular degradation of secretory material and cellular membranes; and (4) the effects of sialographic procedures on the structure of the rat submandibular gland.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $250,092

3.0122, DISEASES OF THE SALIVARY GLANDS AND PANCREAS - VIRUS-INDUCED DIABETES

A.L. Notkins, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Laboratory of Oral Medicine, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00080-06 LOM)

Diabetogenic variants of encephalomyocarditis virus, Coxsackievirus B, and reovirus have been studied in vitro in beta cell cultures and in vivo in animal model systems. One of these variants, a Coxsackievirus B4, was isolated from the pancreas of a child who died with acute juvenile-onset diabetes (JOD). The role of the immunologic systems in JOD also is being studied.

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National Inst. of Health,
National Inst. of Dental
Research $295,301

3.0123, STUDIES ON SJOGREN'S SYNDROME

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The purpose of this project is to determine the etiology of the autoimmune disease Sjogren's Syndrome. Particularly we studied the basis of clinical, serologic and genetic similarities and differences between Sjogren's syndrome alone and Sjogren's syndrome associated with other autoimmune disease; the presence and physiochemical properties of immune complexes in the patients, the ability of the Fc receptor of their RES to clear immune complexes, and the immunoregulation of primary Sjogren's syndrome.

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3.0124, DIET, HORMONES AND DEVELOPMENT OF RAT PAROTID GLAND

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Groups of rats were prematurely weaned to defined diets that differed in proportions of nutrients and in physical consistency to see if these dietary differences affected their feeding patterns, blood levels of thyroid and corticosteroid hormones and maturation of their parotid glands. The pelleted defined diets supported growth as vigorously as did the pelleted control diet (commercial chow). Rats fed the defined diets in liquid form failed to gain weight but suffered no mortality. The powder form of the high fat, moderate protein and carbohydrate (all lactose) diet supported growth almost as vigorously as did the pelleted diets. Unexpectedly, the powder form of the high carbohydrate (mostly starch), moderate fat and protein diet was rejected by the rats, and an unacceptably high mortality resulted. A more palatable version of a high carbohydrate diet will be sought, e.g., by increasing the fat content, in order to minimize partial inanition as variable. The stomach contents, parotid glands and serum hormones of these animals currently are being analyzed. It is anticipated that the next major experiment can be started next April.

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3.0125, INVESTIGATIONS OF SALIVARY GLAND HISTOLOGY, HISTOCHEMISTRY AND SALIVARY PROTEINS OF THE CHACMA BABOON

J. Hattingh, University of the Witwatersrand, School of Dentistry, Dept. of General Physiology, *Jan Smuts Ave., Johannesburg 2001, Transvaal, South Africa*

Baboons are used more and more as models in various branches of Dental Research. However, no baseline values concerning salivary protein content, electrophoretic fractions, salivary flow rates, salivary gland histology and histochemistry, etc., are available. The purpose of the present project is to investigate the above in order to establish these values for both mixed saliva and saliva obtained from the different salivary glands, and in addition to correlate this with salivary gland structure.

SUPPORTED BY

(No Supporting Organization Reported)	funds n.a.

3.0126, THE EFFECT OF STRESS ON CARCINOGENESIS OF SALIVARY GLANDS

M.L. Rins de David, Universidad Nacional de Cordoba, Facultad de Odontologia, Catedra de Fisiologia, *5000 Cordoba, Argentina*

The influence of hormones and pharmacons on salivary glands was studied by different authors.

This work was carried out to observe if stress induced by cold, 15 degrees Celsius, 10 min per day, was able to modify time or characteristics of carcinogenesis of salivary glands induced by DMBA. The action of a stress stimulus does not modify any histological aspect of normal rats in spite of the fact that the levels of plasmatic corticosterone in these experimental animals were higher than the normal levels in these animals.

The data pertaining to experimental carcinogenesis and stress are being computed at present.

SUPPORTED BY

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3.0127, EXPERIMENTAL ONCOLOGY PATHOLOGY IN SALIVARY GLANDS MICE BY MEANS OF THE USE OF 9-10 DIMETHYL-1-2 BENZANTHRACENE

M.M. Fonseca, Universidad Nacional de Cordoba, Facultad de Odontologia, Dept. of Pathological Anatomy, *5000 Cordoba, Argentina*

Morphological and histochemical patterns in glycoconjugated complex substances are to be established in submaxillary and sublingual glands. After determining the time of speediness of reply and the degree of sensibility to drug in both of glands, the same are to be appraised in experimental aspects such as stress and actually by means of the use of sexual hormones.

SUPPORTED BY

Universidad Nacional de Cordoba	$3,500

3.0128, HISTOCHEMICAL CHARACTERIZATION OF MUCOPOLISACCHARIDES COMPLEX SUBSTANCES IN HUMAN SALIVARY GLANDS PATHOLOGY

H. Gendelman, Universidad Nacional de Cordoba, Facultad de Odontologia, Dept. of Pathological Anatomy, *5000 Cordoba, Argentina* (090)

The object of the project is to detect and to characterize glycoconjugated complex substances in human salivary glands with different pathology by means of histochemical resources, in morphologically identified areas and the cell surfaces.

SUPPORTED BY

Universidad Nacional de Cordoba	$3,000

TUMORS & OTHER DISEASES OF SALIVARY GLANDS - PATHOLOGY

3.0129, METHODS FOR THE ULTRACYTOCHEMICAL DEMONSTRATION OF ENZYMES AND BIOMACROMOLECULES OF ORO- AND CRANIOFACIAL TISSUE

J.S. Hanker, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Oral Surgery, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130196)

For summary: see 2.0071.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$18,469

3.0130, ULTRACYTOCHEMICAL AND IMMUNOCYTOCHEMICAL STUDIES OF PERIPHERAL NERVES OF THE OROFACIAL REGION

J.S. Hanker, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Oral Surgery, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130197)

For summary: see 1.0183.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$3,518

3.0131, STUDY OF SALIVARY GLAND STRUCTURE AND FUNCTION

C.A. Schneyer, University of Alabama in Birmingham, School of Medicine, Dept. of Physiology & Biophysics, *1919 7th Ave. S., Birmingham, Alabama* 35233 (R01 DE 02110-15)

This research is concerned with autonomic regulation of growth responses and secretory activity of salivary glands. The role of the two branches of the autonomic nervous system has been more sharply delineated, since under conditions where glandular activity is varied by diverse means of diet, sialadenectomy, administration of autonomic drugs, or ones that have actions on autonomic fibers, the pronounced role of cholinergic as well as beta adrenergic receptors in mediation of the growth changes in being shown.

Secretory activity is being investigated using in vivo whole gland, in vivo duct perfusion, and in vitro duct perfusion. The transport of electrolytes in the main duct will be considered from both luminal and contraluminal aspects, and the role of the autonomic innervation of autonomimetic drugs in the regulation of electrolytes will be examined. Net fluxes of electrolytes and transductal PD will be examined under these conditions.

The whole parotid will be used for extensive examination of neural regulation of certain ions and proteins that have been found to be secreted together across the luminal membrane. The generality of this relationship with diverse kinds of autonomic stimulation is being delineated.

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SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$56,830

3.0132, ION TRANSPORT IN SALIVARY GLANDS

M.E. Fritz, Emory University, School of Dentistry, Dept. of Periodontology, *106 Forest Ave. N.E., Atlanta, Georgia* 30303 (R01 DE 02879-09)

Previous reports from this laboratory have demonstrated a technique for culturing feline parotid acinar cells on collagen gels. Feline acinar cell cultures have been assayed for cell viability by: 1. Exclusion of vital dyes; 2. Light and electron microscopy to determine morphology; 3. Cellular growth determined through formation of monolayers and by DNA assays; and 4. Lack of amylase release into the culturing medium without stimulation. Viral infection with feline rhinotracheitis, a herpes virus, has been correlated with indirect fluorescent antibody procedures, cyclic AMP and GMP measurements, and potential measurements. The results of these studies indicate that 18-24 hours post-infection with herpes virus, cells demonstrate ballooning of the nucleus and regions of thickening in nuclear membranes. In addition, presence of viruses is noted in electron microscopic observations. Infected cells also show membrane potential measurements which are significantly less negative than those found in control cultured cells (X control cells equals -50.8 plus or minus 6.8; X virally infected cells equals -18.9 plus or minus 7.9 S. D. mV), and cyclic AMP measurements which are also less than found in control cells (X control cells equals 5.5 plus or minus 1.2; X virally infected cells equals 4.2 plus or minus 1.0 S. D. pmoles CAMP per 10 to the 6th power cells). The physiologic mechanisms underlying these changes will be examined.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $92,362

3.0133, STUDIES ON PROLINE-RICH SALIVARY PROTEINS

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Saliva is a complex body fluid containing many proteins of both glandular and nonglandular origin. The nature and function of salivary proteins in oral physiology have to be more fully understood and defined in biochemical terms if one is to adequately understand the events which lead to pellicle and plaque formation. Studies in our laboratory resulted in the isolation and partial characterization of a group of proline-rich proteins from human parotid saliva. These highly soluble proteins are of special interest because they exhibit a high affinity for hydroxyapatite, contain phosphate, show genetic polymorphism and display in many respects fascinating similarities to structural proteins such as collagen and enamel protein. It is, therefore, our aim to elucidate the chemical characteristics of these unusual proteins. In this endeavour we will investigate a) the primary structure of all four proline-rich proteins, b) their relationship to collagen and related proteins using proteolytic enzymes such as collagenases, c) their secondary and tertiary structure by circular dichroism, d) the genetic polymorphism on a molecular level and e) the biosynthesis and fate of these proteins upon their release into the oral cavity. Insofar as possible antisera against these proteins will be used to locate their biosynthetic pathway in tissue culture systems and to quantitate their content in oral fluids in both normal and diseased subjects. Our overall objective is, therefore, to fully understand the chemistry and structure of this unique group of proteins, which will enable us to conduct comparative studies with proteins of the connective tissue class and facilitate the elucidation of their role in nature and certain oral diseases.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

3.0134, GENETIC POLYMORPHISMS OF SALIVA

E.A. Azen, University of Wisconsin, Madison Campus, Medical School, Dept. of Medicine, *307 N. Charles St., Madison, Wisconsin* 53706 (R01 DE 03658-15)

Structural studies on Pb proteins of the common and variant genetic types will be continued by performing sequential analysis. Monkey Pb proteins will also be studied by sequential analysis for the purpose of a biochemical evolutionary comparison. Possible functions of Pb and Pr-Db proteins will be studied by looking for a relationship between Pb and Pr-Db variant types and the incidence of caries and/or periodontal disease. Attempts will be made to determine cellular and subcellular localization of the Pb proteins using immunofluorescence techniques. Attempts will be made to identify new genetic polymorphisms in human saliva using sensitive protein staining methods, high-voltage starch-gel electrophoresis techniques and radio-labeling of trace protein components followed by autoradiography. We will continue linkage studies of Pb and Pr-Db systems with many known genetic markers in order to assign them to specific linkage groups.

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SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$34,537

3.0135, IMMUNOPATHOLOGY--EXPERIMENTAL AUTOALLERGIC SIALADENITIS

S.C. White, University of California, Los Angeles Campus, School of Dentistry, Section of Oral Radiology, *405 Hilgard Ave., Los Angeles, California* 90024 (R01 DE 03859-06)

The purpose of the proposed research is to study the activity of cytotoxic and inhibitory immunopathologic mechanisms operating in EAS and in patients with Sjorgren's Syndrome. In the first experiments, cell-mediated cytotoxicity (CMC), antibody-mediated cytotoxicity (AbC), and antibody-dependent cell-mediated cytotoxicity (ADCC) activity will be measured in lymphocytes and sera of rats during the course of EAS. Additionally, inhibitory antibody blocking activity and suppressor cell activity will be measured during recovery from EAS. Cytotoxicity will be measured by reacting immune sera or lymphocytes in vitro with Cr-51 labeled submandibular gland target cells and measuring target cell lysis by release of Cr-51 from killed cells. Additional experiments will measure the cytotoxic CMC, AbC, and ADCC activities and antibody blocking and suppressor cell activities in animals protected from development of EAS. Resolution of EAS lesions or protection from lesions may be mediated by activation of inhibitory processes which turn off cytotoxicity. The tissue specificity of the cytotoxicity and inhibitory reactions will be measured during the development of EAS by testing immune lymphocytes and sera with target cells prepared from several organs and rat strains. It is hoped that sufficient definitive information will be gained to provide an increased understanding of the immunopathologic mechanisms operating in EAS.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$61,970

3.0136, SALIVARY GLANDS AND THEIR INNERVATION IN DIABETES

J.S. Hanker, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Oral Surgery, *Chapel Hill, North Carolina* 27514 (R01 DE 04730-02)

This project is to study the effects of diabetes mellitus on salivary glands and their innervation. Our previous studies have shown a decrease in size of the submandibular gland of the male mouse due to diabetes. In addition, the granular tubules have less amylase granules, and less of the volume of the gland is occupied by ducts. We have observed a Schwann cell proliferation in trigeminal ganglia of the C57BL/KsJ-Db mice afflicted with diabetes mellitus. The diabetic mutants provide a useful experimental model for the evalution of these effects. The changes observed in their salivary glands and the trigeminal ganglion could be relevant to the increased caries and periodontal involvement. The secretory activity of the salivary glands, regulated by acetylcholinesterase-positive parasympathetic fibers from branches of the fifth, seventh, ninth and tenth cranial nerves, will be assessed by examining the fibers with a precise histochemical method for acetylcholinesterase. The changes in the ductal portions of the submandibular gland will be evaluated with various histocytochemical methods including immunocytochemical methods for nerve growth factor and glucagon. The extent of the peripheral neuropathy, especially as it affects the trigeminal ganglion, and trigeminal and facial nerves will be assessed with various neurohistochemical methods including those which demonstrate axonal transport and capillary permeability. The caries, plaque accumulation periodontal changes and changes observed in the tongue of the diabetic mice suggest that this mouse model may be of value in studying the oral effects of the disease.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$70,306

3.0137, KERATINIZATION OF NORMAL AND ALTERED EPITHELIUM

B. Singh, Medical College of Georgia, School of Dentistry, Dept. of Oral Pathology, *1459 Gwinnett St., Augusta, Georgia* 30902 (R23 DE 03655-03)

Objectives of this study will be to obtain information about protein synthesis in the hamster cheek pouch in relation to epithelial cell differentiation, under normal and altered conditions. 1) Particular attention will be paid to the role of protein(s) synthesized in the upper cell layers of the epithelium and how they relate to the cell organelles with particular attention to the keratohyalin granules, 2) Correlative histochemical, light and electron microscopic autoradiographic studies will be carried out to identify the sites of active protein synthesis. For this purpose a series of tritiated precursors will be used, 3) Studies to determine the biochemical nature of the proteins in relation to the keratohyaline granules will also be conducted, 4) The nature of the epithelia altered by dimethylbenz(a)anthracene (DMBA) will also be characterized by the abovementioned techniques and compared with normal epithelia, 5) Attempts will be made to define the differences between normal and altered human epithelia in the hopes of establishing data that may be used as a diagnostic parameter, 6) Detailed ultrastructural characterization of the normal hamster cheek pouch epithelium will be carried out. If the objectives of this study can be achieved, then a significant step can be made toward understanding the mechanisms of differentiation of epithelium under normal and neoplastic conditions.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

3.0138, A CELL CYCLE STUDY OF DEVELOPING RAT SALIVARY GLANDS

R.M. Klein, University of Kansas, Medical Center, School of Medicine, Dept. of Anatomy, *39th St. & Rainbow Blvd., Kansas City, Kansas* 66103 (R23 DE 04557-02)

Acinar cell differentiation continues postnatally in the rat salivary glands and involves a cell proliferative growth period during its early stages. Cells which are undergoing division are passing through a cycle of events including DNA synthesis, visible mitosis, and the preparatory phases which preceed these periods. This cell cycle can be measured by use of autoradiography and provides a model by which one can study the effects of the autonomic innervation (parasympathetic and sympathetic) on the growth and development of the rat salivary glands (parotid, submandibular, and sublingual).

This study will analyze the role of autonomic nervous system (A.N.S.) in the development of the salivary gland by stimulation and diminution of both sympathetic and parasympathetic branches. This will be done by the use of sympathomimetic, parasympathomimetic, sympatholytic, and parasympatholytic drugs as well as by actual surgical denervation procedures and chemical sympathectomy. The normal cell cycle curve of each of the major salivary glands will be used as a foundation upon which alterations produced by drug or surgical procedures may be determined.

In addition to the measurements of the duration of the acinar cell cycles phases, thymidine labelling index, mitotic index, DNA, RNA, protein and incorporation of 3H-thymidine (scintillation counting) will be calculated in order to further elucidate the importance of both branches of the autonomic nervous system in cellular events. These experiments will provide a basic understanding of the role of the A.N.S. in the development of the rat salivary glands.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $13,036

3.0139, IN VITRO STUDIES OF SECRETORY CELL STRUCTURE AND FUNCTION

C. Oliver, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Experimental Morphology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00199-03 LBS)

Secretory processes in several cell types are currently under investigation. Cell dissociation and short term culture (up to 1 month) methods have been established for rat exorbital lacrimal, parotid and pancreatic acinar cells. These cultures are being used to study various aspects of the secretory process. Initial emphasis is being placed on morphological, cytochemical and biochemical characterization of the cultured cells. Additionally, uptake of horseradish peroxidase and internalization of 125I labeled cell membrane are being investigated, in vivo and in vitro. The events involved in matrix deposition by cultured odontoblasts, and melanosome formation in cultured neural crest cells, are also being studied.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $94,560

3.0140, SALIVARY SYSTEMS

R.O. Wolf, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Oral & Pharyngeal Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00217-02 CI)

This project is concerned with mechanisms of production and control of extrinsic (i.e. saliva) and intrinsic (e.g. serum salivary isoamylase) salivary gland products. A. Human (primarily parotid) saliva chemical consitiuents and mechanisms are evaluated as related to health and disease. Parotid salivary flow rate, protein composition and enzymes (particularly lysozyme and amylase) are evaluated in normals and selected disorders such as Sjogren's syndrome and aphthous stomatitis. B. The intrinsic secretion of salivary isoamylase in serum of cystic fibrosis of the pancreas and Sjogren's syndrome as well as normal monkey serum and monkey gland homogenates is being studied. Diagnostic application and an understanding of the mechanisms of hyperamylasemia are being sought. C. Fluoride is being studied as a sialogogue for prevention and alleviation of xerostomic symptoms.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$84,800

3.0141, RELATIONSHIP OF ORAL PERCEPTION AND SALIVA BIOCHEMISTRY TO HEALTH AND DISEASE

R.P. Feller, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *11201 Benton St., Loma Linda, California* 92357 (605-001-P)

A laboratory to study oral perception and the biochemistry of saliva in both health and disease will be established. Parotid and whole saliva samples, collected from geriatric patients with pathologic, alcoholic or neuropsychiatric disorders will be analyzed systematically and compared to saliva collected from healthy geriatric subjects. Taste sensitivity, frequently altered in age and disease, will be correlated to saliva flow and biochemistry to determine diagnostic and prognostic indicators of disease.

Animal studies will be based on a method for prolonged maintenance of a relatively constant flow rate of parotid and submandibular saliva in the dog. This procedure will be employed to study the pharmacological and physiological effects of specific drugs on salivary function and saliva constituents. The effects of toxic doses of ouabain and digoxin, both cardiac glycosides. will be investigated to enhance information obtained from human studies. Salivary response to other drugs commonly prescribed for Veterans Administration patients, such as isoproterenol, salicylates and diuretics, including meralluride, acetazolamide, sodium chlorthiazide and sodium ethacrynate, all of which are classified differently according to manner by which they alter solute excretion, will be studied.

Finally, it is known that atropine, smoking and blindfolding affect salivary flow and composition in human subjects, and visual deprivation affects gastric secretion in dogs. These parameters and EEG will be monitored in nonsmokers and smokers, whose EEG patterns and salivary electrolyte levels differ. The results of this study may elucidate neural mechanisms involved in the production and secretion of saliva.

We feel that by providing insight into glandular management of salivary constituents, saliva will become an important biomedical monitor.

SUPPORTED BY

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3.0142, AGE-RELATED CHAGES IN SECRETORY CELLS OF THE SALIVARY GLAND

S. Kim, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *2215 Fuller Rd., Ann Arbor, Michigan* 48105 (506-001-P)

Studies of age-related changes in the rat parotid gland have continued. Changes in the cellular contents of secretory proteins with increasing age have been investigated by assaying the level of alpha-amylase activity in parotid glands of rats of different age groups. These studies have revealed that the cellular level of alpha-amylase is highest in the gland of rats about 12 months old but the level declines with age. The amylase activity in the gland of 30 month old rats is about 60 percent of that in the gland of 12 month old rats. Despite these differences, the proportion of secretory proteins (acid insoluble) to total proteins remains at about the same level. Morphologically, the increase in the amount of lipofuscin granules and the heterogeneity in the appearance of the secretory granules are the two most prominent changes which are observed in the gland with increasing age. There were no obvious, qualitative differences among age groups in the cellular organelles which are normally concerned with the secretory protein production. However, the rate of protein synthesis, as indicated by 3H-leucine incorporation declines in 30 month old rats. The rate of protein synthesis in the gland remains about the same between the age of 2 and 18 months. However, the gland slices of 30 month old rats incorporate about 30 percent less than of the younger rats, indicating that protein synthesis is declined in old rats.

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Medicine & Surgery funds n.a.

3.0143, EFFECT OF RADIATION ON SALIVARY GLANDS

M.I. Cogan, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Martinsburg, West Virginia* 25401 (613-001-I)

The purpose of this project is to correlate the values obtained from three specific diagnostic tests used to determine changes in salivary composition and salivary gland function and structure in patients who have received radiotherapy for malignancy of the head and neck area.

Diagnostic tests will be conducted to determine changes in salivary gland function and structure in patients undergoing head and neck radiotherapy. These tests will include the following procedures: salivary flow rate determination, composition of saliva, secretory sialography, salivary gland scanning, and clinical grading.

The results of saliva analysis of the patients suffering from cancer and receiving ionizing irradiation in the head and neck will be reviewed. The serial radiological contrast study of salivary glands in patients before, during, and after head and neck radiotherapy will be of value in defining the secretory changes in irradiated glands. The scintigraphic estimation of salivary glandular dysfunction caused by radiotherapy will then be compared with the results of the other diagnostic tests.

Similarities and differences between trends in the scintigraphy scans and the clinical grading and the salivary flow rates will be noted. Also, the relationships between findings on X-ray film and the scintigraphy will be observed. The correlation noted in this study between the severity of xerostomia and the degree of involvement evident on saligraphy will be reported.

It is felt that an analysis of the data resulting from a correlation of the tests, as described above, will contribute to a more comprehensive understanding of the effects of radiation on the salivary glands.

SUPPORTED BY

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Medicine & Surgery funds n.a.

TUMORS & OTHER DISEASES OF SALIVARY GLANDS

- DIAGNOSIS & TREATMENT

3.0144, SALIVARY CHANGES IN CANCER THERAPY PATIENTS

K. Izutsu, University of Washington, School of Dentistry, Dept. of Oral Biology, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P50 DE 02600-130034)

The proposed work deals with examining the effects of certain cancer chemotherapy protocols on salivary gland function, and attempting to correlate these effects with changes in the oral health of the patients. Salivary flow rates and the concentrations of certain electrolytes and proteins will be measured throughout the treatment period. Changes in oral health will be measured using a standardized visual exam.

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National Inst. of Health,
National Inst. of Dental
Research $81,056

3.0145, THE CAPSULE AS A DELIMITER OF SALIVARY GLAND REPAIR

M. Lorber, Georgetown University, School of Medicine, Dept. of Physiology & Biophysics, *3800 Reservoir Rd. N.W., Washington, District of Columbia* 20007 (R01 DE 04817-02)

The work in progress is an investigation of whether the capsule of the salivary gland plays a role in regulating the repair process following the removal of a portion of the parenchyma from the submandibular or parotid glands. Preliminary observations in the rat and the dog suggest that extirpation of some parenchyma is not followed by scarring but that repair occurs in adults of both species. In rats particularly, it has been noted that local hemorrhage is often followed by atrophy. Therefore, careful surgical and pharmaceutical measures to control hemorrhage are essential. These are in progress and, if successful, will be followed by autoradiography using tritiated thymidine to follow the sequential changes occurring during the healing process. The possibility of a sex difference in the susceptibility of the rat to salivary gland atrophy following surgery will be investigated as will be the possible relationship between capsular topography an the extent of repair.

SUPPORTED BY

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3.0146, SALIVARY GLANDS, POLYAMINES AND CHEMOTHERAPY

D.G. Brown, Southern Illinois University, Edwardsville Campus, School of Dental Medicine, Dept. of Biomedical Sciences, *Edwardsville, Illinois* 62025 (R23 DE 04447-03)

The possible involvement of polyamines in growth, differentiation and neoplasia has stimulated the study of endogenous levels of these compounds (putrescine, spermidine and spermine) and enzymes responsible for their synthesis (ornithine and S-adenosylmethionine decarboxylases). In particular, reports on increased polyamine levels in rapidly growing and neoplastic tissues have prompted a search both for techniques which might be used diagnostically to detect abnormal polyamine levels and for specific inhibitors of polyamine synthesis.

To date, little is known about the polyamines and their synthesizing enzymes in salivary glands or in saliva. In addition, there is little use of chemotherapy for salivary or oral neoplasias and as a result, little is known about specific cytotoxic drug effects in tissues of the oral cavity or salivary glands.

Polyamine and decarboxylase levels and ultrastructural (EM) characteristics will be studied using mouse salivary glands, both normal and those induced to grow by injecting the mouse with isoproterenol (IPR). IPR-induced salivary growth involves both hypertrophy and hyperplasia and is used as a model growth system. The effect of certain antineoplastic drugs on normal and IPR-induced salivary tissues will be studied by correlating the biochemical and ultrastructural characteristics described above. During the study, correlations will be made between the polyamine and decarboxylase levels in the glands, the state of growth of the glands, and the effects of cytotoxic drugs on both the biochemical parameters and the structure/function relationships as observed microscopically.

It is not known if human saliva contains polyamines or their synthesizing enzymes. Saliva will be analyzed to determine if it contains these components in measurable quantities. If present, studies will be performed to examine the feasibility of using such analyses as diagnostic method for assessing salivary gland growth and/or function.

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3.0147, STIMULATION OF REGENERATING RAT SUBMANDIBULAR GLANDS

J.L. Boshell, Medical College of Georgia, School of Dentistry, Dept. of Oral Biology, *1459 Gwinnett St., Augusta, Georgia* 30902 (R23 DE 05072-01)

Regeneration of rat submandibular glands following partial extirpation of the gland apparently has not been seen to go to full completion. The appearance of the normal numbers of mature granular duct cells was not reported in any of the studies. One possible explanation is that the experiments were not extended an adequate length of time in order to make the observation. Another is that complete regeneration doesn't take place. These proposed experiments will hopefully give more information about the regenerative ability of salivary glands. A portion of the left submandibular gland will be removed from each experimental animal. Isoproterenol will be given to one group of rats after surgery to see if complete regeneration can be achieved and/or speeded up. Testosterone will be given to another group following surgery and its effects will be observed. A third group will be given both isoproterenol and testosterone after surgery. Appropriate controls will be run with each group. Effects of the agents on the glands will be studied using histologic, histochemical, morphometric, and electron microscopic techniques. The rate of appearance of mature parenchymal cells will be monitored. Their numbers will be counted and compared to known well documented adult values as well as control values. Because of the need for normal functioning salivary gland tissue, this type of experimentation has both clinical and biological significance. Furthermore, isoproterenol and testosterone have been shown to have profound effects of developing and mature rat submandibular gland morphology, histochemistry, and biochemistry. Therefore, it is expected that administration of either or both of these agents will cause significant change in regeneration of rat submandibular glands following partial extirpation.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$18,557

3.0148, CHEMOTHERAPY AND IMMUNOTHERAPY FOR CARCINOMA OF THE HEAD AND NECK

A.A. Neshat, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Oncology Surgical Section, *Asheville, North Carolina* 28805 (637-006-F)

So far twenty-two (22) patients have been entered into this Protocol. From these twenty-two (22) patients, one is still living and twenty-one (21) patients have died. The analysis of the survival shows that the shortest survival was seven (7) weeks and the longest survival was eighteen (18) months. The average survival was seven (7) months.

The Chemotherapy and Immunotherapy did not really increase the survival of these patients but it appears to be a palliative measure for these patients. The majority of the patients felt better; they gained weight; and they were able to swallow liquids and solid foods and had less pain. In some of the patients we noticed considerable response locally. Some of the tumors in the skin or subcutaneous sloughed off and those patients who had lesions inside the mouth or throat were able to spit our pieces of the necrotic tumors. None of the patients complained about their BCG vaccination sites and it seems that the vaccination with BCG was tolerated satisfactorily.

This pilot study has been ended and the conclusion has been drawn that chemotherapy and immunotherapy is an effective palliative measure for treating patients with extensive head and neck cancer.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

3.0149, BIOCHEMISTRY OF THE ORAL FLUIDS IN HEALTH AND DISEASE

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Major emphasis has been placed upon development of a high-performance saliva substitute particularly for use by patients who have received radiotherapy for malignancy of the head and neck area. The material is, of course, appropriate for patients with xerostomia of any etiology but the radiated patient is the principal concern. We have authenticated by clinical trial that our present formula VA-OraLube completely relieves the soft tissue problems associated with dryness of the mouth. Publications have dealt with irradiated patients and with psychiatric patients. The Ca, P and F concentrations have now been adjusted to provide a high level of remineralization of damaged tooth surfaces in the xerostomic patients. We have found that 2.0 ppm fluoride serves this function admirably. We have also examined the critical nature of the interval between dental extraction and initiation of radiotherapy and have altered our approach to these patients as a result. Also established has been the effect of radiotherapy on whole saliva flow as well as the isolated secretion of the parotid gland, We have also found that irradiation does not have a direct deleterious effect on dental enamel and solidified the concept that is indeed salivary flow deprivation that induces the ravaging form of dental disease characteristically seen in xerostomic patients.

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3.0150, SALIVARY CYCLIC AMP IN IRRADIATED PATIENTS

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This pilot study investigates the changes in excreted salivary cyclic nucleotides in patients irradiated for oral malignancies. Since cyclic nucleotides govern many cellular activities in all living organisms and some of these activities may bring about morbid changes in humans, it was postulated that post-irradiation morbidity may be related to changes in salivary cyclic nucleotides. Salivary samples were procured before, during and after cobalt therapy from four male patients. These samples were transferred in a frozen state to the Department of Physiology, U.S.C. School of Dentistry for cyclic AMP and GMP assays. Results of these analyses demonstrated in most cases there was a general rise in levels of cyclic nucleotides following radiation therapy. Further study is being instituted at this time to support this small sample. If increase in these compounds are definitely established following irradiation, then health care personnel can counteract these changes by phosphodieterase inhibitors which will block the over production of cyclic nucleotides.

SUPPORTED BY

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3.0151, USE OF RADIOACTIVE PHOSPHORUS IN EARLY DIAGNOSIS OF RECURRENT CARCINOMA OF THE HEAD AND NECK

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This project is continuing. However, we are now using bleomycin-indium 111 as a tracer. We have studied some 20 patients to date and have found a 100% positive test rate in this group of head and neck cancers ranging in size from 1 cm to 8 cm. We have had several false positive tests in the area of recent surgery, and mandibular exposure. It is felt that with further purification of the bleomycin-indium 111 that the background counts will decrease and the scanning agent will become even more specific for carcinoma.

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TUMORS & OTHER DISEASES OF SALIVARY GLANDS - PREVENTION

3.0152, EFFECT OF PAROTID FUNCTION ON SALIVA AND CELLS

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The parotid glands of rats have been shown to be profoundly affected by increased or decreased mastication of food. With reduced mastication (a liquid diet), there is gland atrophy. With enhanced mastication (a bulk diet), there is gland enlargement. We have investigated the effects of enhanced and reduced mastication on the protein composition of parotid saliva. When gland enlargement is stimulated by increased mastication of food, there are parallel increases in the saliva concentration of protein and of three secretory enzymes (amylase, RNase and DNase). Electrophoretic profiles in anionic, cationic and SDS acrylamide gels show no additions or deletions of bands and no major differences in the quantity of stained material in each band. In contrast, there are striking alterations in the protein composition of the parotid saliva of rats fed a liquid diet. There are non-parallel decreases in the three enzymes and in protein. Cationic and SDS acrylamide gels indicate that three major proteins are absent. We will isolate from the saliva of control animals the proteins that are missing in the saliva of rats fed the liquid diet. We will determine several biochemical properties of these proteins, their molecular weight, their amino acid composition and their isoelectric points. These proteins are currently of special interest because of their unusual composition. They are basic proline-rich proteins and three acids--proline, glycine and glutamic acid/glutamine--comprise more than 75% of their total amino acid residues. Preliminary findings indicate that certain acidic proline-rich proteins are also affected when mastication is reduced. We will devise procedures to isolate and identify these proteins and to then determine the manner in which they are affected by altered mastication.

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3.0153, NUTRITIONAL FACTORS IN ORAL ULCERS - ZN, B12, FOLATE

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OBJECTIVES: The major objectives of this study are to determine the effectiveness of a zinc sulfate nutritional supplement as a preventive or cure for recurrent idiopathic oral ulcers (recurrent aphthous ulcers) and to evaluate the levels of folic acid and vitamin B12 with respect to the occurrence of these ulcers. A further objective is to evaluate in these patients the levels of some other trace metals including cadmium, manganese, copper and chromium which may compete metabolically with zinc.

METHODS: Diagnosis of the idiopathic oral ulcers will be made on the basis of history, clinical examination and other necessary confirmatory means such as cytology, biopsy or culture. Other similar types of ulcers or lesions will be ruled out by serology, complete blood counts or chemistries as necessary. Plasma zinc, iron, copper, cadmium, manganese and chromium determinations will be done as well as serum or RBC folic acid and serum vitamin B12. Patients will be provided zinc sulfate and placebo supplementation on a double blind basis. The trace metals and vitamin levels being studied will be monitored regularly for changes. Duration, frequency, numbers and size of the ulcers which occur will be observed. Patients found to have folate or vitamin B12 deficiencies will be treated appropriately for these in addition to the zinc or placebo supplementation.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $38,966

3.0154, PHARMACOLOGY OF SUBMAXILLARY GLAND SECRETION IN VITRO

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We are studying the pharmacological aspects of ion and mucous secretion in the rat submandibular gland. Rat submandibular gland cells are isolated using a chromatographically purified collagenase and hyaluronidase and the pharmacological aspects of submandibular secretion is evaluated in terms of (1) the receptor mediated, physiological response to cholinergic and adrenergic agonists. This is accomplished by determining the net efflux of K and the amount of 14C-glucosamine labeled mucin released into the cell suspension media following parasympathomimetic and sympathomimetic stimulation. (2) The changes in the levels of cyclic AMP and cyclic GMP following stimulation are determined and then correlated with the receptor mediated, physiological response of these cells with and without the addition of phosphodiesterase inhibitors.

The method developed for the isolation of rat submandibular cells results in the isolation of the principal secretory cells in their natural functional units and they demonstrate a high degree of sensitivity to various secretagogues tested.

These studies are intended to improve our understanding of the membrane mediated and subsequent intracellular events that are thought to be important in the stimulus-secretion coupling mechanism in this gland.

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Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $44,901

3.0155, HUMAN SALIVARY ANTIGENS - CHARACTERIZATION

M.J. Levine, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (R01 DE 04971-01)

Salivary glycoproteins and proteins are recognized as having a significant role in the ecology of the oral cavity. Alterations or abnormalities of these macromolecules may occur in periodontal disease, dental caries, and cystic fibrosis. In this study, we propose to purify and biochemically and immunologically characterize selected glycoproteins and proteins of human and primate salivas and to compare components from normal persons with those with dental disease and patients with cystic fibrosis.

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DENTAL PULP STUDIES - ETIOLOGY

3.0156, REVIEW OF THE COLORING METHODS FOR THE STUDY OF THE MYELINIC AND AMYELINIC NERVOUS FIBERS OF THE HUMAN TOOTH

C.G. deCaceres, Universidad Nacional de Cordoba, School of Dentistry, Dept. of Anatomy, *University City, 5000 Cordoba, Argentina*

This piece of work includes a review of the coloring techniques for the study of the myelinic and amyelinic nervous fibers in the dental pulp and its final behavior including their classic and special coloring techniques.

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DENTAL PULP STUDIES - PATHOLOGY

3.0157, CIRCULATION STUDIES IN TEETH AND SUPPORTING STRUCTURES

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The overall objective is to increase our knowledge about the circulation and hemodynamics in oral and related tissues of an animal model. The specific aims involve a multi-technique approach to: 1. determine local blood flow, tissue O2 consumption pulpal pressures, and other related variables to assess effects of surgical and transplant procedures for correcting abnormalities from genetic, injury or disease origins; 2. assess fiberoptic photoplethysmography and an isothermal flowmeter for possible clinical application; and 3. improve and expand our computer capability. The indicator dilution and the radioactive microsphere methods will provide assessment of local blood flow. The submarine respirometry approach will be used to determine O2 consumption. The pulpal pressure determinations involve a tonometric and/or a direct cannulation approach. The achievement of our objectives will furnish further knowledge of basic physiology and new ideas for future studies.

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Services, Public Health Service,
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National Inst. of Dental
Research $92,103

3.0158, DEMONSTRATION AND DISTRIBUTION OF THE LYMPHATICS IN THE PULPAL AND PERIAPICAL TISSUES

W.C. Bird, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *1201 Broad Rock Rd., Richmond, Virginia* 23249 (652-002-F)

The purpose of the investigation was to study the distribution of lymphatics and associated small caliber blood vessels in the dental pulp and periapical region of the dog utilizing orthograde and retrograde perfusion of a carbon suspension.

The project 'Demonstration and Distribution of the Lymphatics in the Pulpal and Periapical Tissues' has recently been terminated. The investigators utilizing various infusion methods, pressures, and time periods were unable to introduce the carbon suspension into oral tissues in a retrograde fashion via the cervical duct. The major problem was extravasation even under low pressure. Though Not the objective of the study, it was possible to introduce the suspension in a supra-pulpal (orthograde) fashion via near-exposed class V cavity preparations of deliberately inflamed pulps and recover the suspension in the regional cervical lymph nodes within two hours. This latter observation deserves more study.

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DENTAL PULP STUDIES - DIAGNOSIS & TREATMENT

3.0159, PULPAL SOUND AS A DIAGNOSTIC TEST OF PULP VITALITY

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Present tests of endodontic vitality are of limited value. All depend on nervous vitality which is a questionable approach. Nervous vitality is not essential to pulp vitality while blood flow is essential. Therefore the objective of this study of pulpal blood flow can be determined and used as an index of pulp vitality.

Two experimental listening devices will be tested-a surface transducer system which directly monitors acoustic vibration and an ultrasonic doppler system. The sound systems will be compared against electric and cold pulp testers in 25 patients. Teeth not responding to electric and cold pulp testers will receive 'test preparations.' results from all methods will be correlated and cross tabulated.

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3.0160, EVALUATION OF EXPEDIENT PROCEDURES FOR TREATING DENTAL PULP DISEASE IN NAVAL PERSONNEL

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TECHNICAL OBJECTIVES: Pulp disease is the most common cause of dental emergencies in Navy and Marine Corps populations. Microbial toxins and restorative procedures can injure the dental pulp to such an extent that healing is not possible. The pulp's demise is often protracted and undetected until the sudden onset of severe pain and abscess. The individual is then incapacitated. Exacting and time-consuming treatment by root canal filling is the only predictable means presently available for saving these teeth. The purpose is to develop methods to nullify toxic and harmful restorative effects on pulp tissue, develop fast, uncomplicated alternatives to root canal filling or extraction and establish diagnostic criteria for determining which pulp-diseased teeth may be reliably treated by these methods.

APPROACH: Efficacy of current techniques and materials for treating teeth with pulp disease in naval dental clinics will be evaluated by comparing the thorough preoperative diagnosis with long-term results of therapy. Health status of dental pulp as determined microscopically for condemned teeth, will also be correlated with their clinical analysis. Toxicity of microbial components in dentin will be evaluated intradermally in rabbits, with cultured cells, and in primate teeth. From these studies guidelines will be established for a two-year clinical study for the diagnosis, prognosis, and expedient treatment of pulp disease.

PROGRESS: For this period, 415 incoming naval recruits have been examined. Sixty-eight of these patients had 107 teeth with deep caries that extended through at least 3/4 the dentin, but short of pulp exposure. For all of these pulp-diseased teeth, results of a thorough clinical examination, tests and history were recorded, as well as comprehensive treatment data and short-term follow-up exams. Sixteen teeth in this group were condemned to extraction and 12 of these were recovered for histologic evaluation. One (1) technical report.

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3.0161, PULPAL RESPONSE TO RESTORATIVE PROCEDURES AS APPLIED DURING DENTAL TREATMENT IN NAVAL PERSONNEL

W.R. Cotton, U.S. Dept. of Defense, Navy, Naval Medical Research Inst., Dental Sciences Dept., *Bethesda, Maryland* 20014 (DN877444)

TECHNICAL OBJECTIVE: Approximately one-half of the dental emergencies in Vietnam originated from symptoms arising from pathology of the dental pulp. This pathology may be aggravated by, or even produced by, dental treatment procedures. The necessity of avoiding such emergencies is of paramount importance in operational situations where treatment by naval dental officers is not available, such as aboard submarines, most surface ships, and at isolated Navy and Marine Corps activities. It is the intent of this project to evaluate useful materials and treatment procedures for their potential to cause or aggravate pathological conditions of the dental pulp. Specifically, this study will evaluate the effect of a cavity drying agent on the pulp. Should this material prove to be non-toxic to the dental pulp, it can be assumed that it will not be a contributing factor to the incidence of dental emergencies in Navy and Marine Corps personnel, and can be recommended as a safe, expedient, and cost-effective treatment procedure.

APPROACH: Cavity preparations will be prepared on the buccal surfaces of human noncarious teeth to be extracted for orthodontic reasons. The experimental specimen will be treated with an acetone/ether drying agent prior to insertion of a filling. The contralateral control tooth will have the same treatment except that no drying agent will be applied. The specimens will be evaluated microscopically at postoperative intervals of 1-3, 7-12, and 21-30 days.

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3.0162, ENDODONTIC EXTRUSION - EFFECT ON THE PERIODONTAL LIGAMENT AND SUPPORTING STRUCTURES

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Clinical and histological observations were made on three dogs at post extrusion intervals of two, four, and seven weeks. At two weeks radiolucent areas were seen surrounding the roots. Radiographically, the radiolucent areas seen during extrusion appeared normal by the fourth week. Clinically gingivitis from debris and lack of crown contour and some 'rolling' of the attached gingiva were observed. Histologically, at 7 weeks new bone was formed at the alveolar crest, interradicular and apical areas. The periodontal ligament was virtually normal after 7 weeks. No large areas of resorption or nonreattachment of periodontal ligament was observed. From the clinical and histological findings in this study vertical extrusion of teeth is an acceptable procedure.

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IV. CRANIOFACIAL ANOMALIES, GENERAL

EPIDEMIOLOGY

4.0001, DATA BANK - COMPUTERIZATION OF CLINICAL DATA

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Forms suitable for electronic data processing have been developed for use by our specialists. A survey form (Physical Systems) which describes the initial state of each of our patients has been developed and is being completed for the entire clinic population.

7 of which are completed and being kept current. 1. Names: patients' names and CCFA numbers. 2. Demographic: identifies patients, shows date first seen, referral source, patients's home, and patient category. 3. Physical Systems: identifies patient and describes initial state of all patients on whom clinic has sufficient data to warrant it. 4. Inventory: catalog of information available on each patient, ages at which patient was seen, relationship to proband if a family member prints out inventory record to be kept in patient's file. 5. Census: generates reports for any given time period on numbers of patients who have been through the clinic and how many patients each specialist has seen. 6. Search other files and collect data for special studies; i.e., congenital palatopharyngeal incompetency, audiometrics, hemifacial microsomia, tomograms, muscle function, type of surgery, and referral sources, age at referral and presumptive diagnosis.

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4.0002, DATA BANK - CCFA

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The objective of the CCFA Data Bank is the development of an electronic data processing system designed to facilitate the storage, retrieval and analysis of clinically important information. The design of the system was dictated by present and anticipated user needs. The first objective was to build files of general diagnostic data including demographic information, then adding more detailed information on various systems. In keeping with the open ended system and allowing for expansion, we have added files on growth studies, surgical history and speech examination. Next we will build a file of data from speech exams which have been collected over the past eight years and which have not previously been stored in readily analyzable form. Data in research files are analyzed using various statistical programs and complex searches of multiple files to identify unique patient groupings are performed.

Cephalograms of all the clinic's CPI (Congenital Palatopharyngeal Incompetence) patients and our group of Normal Controls have been digitized using the CPI protocol. These data are now being analyzed. The CPI protocol was also applied to a study of the pharyngeal area of Aperts and Crouzon's patients which was completed this year. Our digitizing capability is now being used for a longitudinal study of the growth of the tonsils and adenoids in various cleft types and in our group of normal controls.

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ETIOLOGY - DEVELOPMENTAL BIOLOGY

4.0003, EPIGENETIC REGULATION OF ENAMEL PROTEIN SYNTHESIS DURING EPITHELIAL-MESENCHYMAL INTERACTIONS

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The basic objective of the sub-program is to identify and monitor the quality and quantity of specific gene products which characterize the phenotype of the inner enamel epithelium, preameloblasts and ameloblasts during fetal and postnatal tooth development. These experiments hypothesize that several types of collagen, proteoglycans and enamel proteins (i.e. amelogenins) are synthesized and secreted by the inner enamel epithelium during differentiation into secretory ameloblast cells. It is further suggested that intracellular species of these specific gene products exist as higher molecular weight, precursor species. These experiments utilize several strains of mice and New Zealand white rabbits. These studes employ experimental embryological methods, cell and tissue culture, pulse/chase labeling studies, several synthesis and secretion inhibitors, protease inhibitors, biochemical and immunological methods. In addition to characterization of these macromolecules, additional studies are designed to isolate and characterize the messenger RNAs found within inner enamel epithelial cells during differentiation into secretory ameloblasts. This strategy enables precise characterization of the specific gene products prior to post-translational modifications and also will enable the production of cDNA complementary to collagenous and non-collagenous proteins. This molecular data will further enable critical dissection of several significant congenital dental deformities including amelogenesis imperfecta as well as major congenital craniofacial malformations which have associated tooth aberrations.

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Research $108,542

4.0004, EMBRYONIC BASAL LAMINA DEVELOPMENT

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The objective of this subprogram is to characterize the embryonic and fetal basal lamina associated with developing tooth organs in vivo and in vitro. The role of the basal lamina in development, especially morphogenesis, is evident but not as yet established. We assume the tooth morphogenesis, especially epithelial-mesenchymal interactions, may be mediated by continuously changing properties of the basal lamina located on the undersurface of the inner enamel epithelium. We assume further that tooth organ morphogenesis such as cusp formation in the molar analagen is effected by the basal lamina (e.g. structure and function). Therefore, these experiments attempt to describe in detail the biochemical composition, temporal synthetic activities associated with the lamina, remodeling of the lamina, and the establishment of the functions of the basal lamina during tooth morphogenesis in highly inbred strains of mice. Further, studies are planned to assess these characteristics of the lamina in steroid-induced congenital craniofacial malformations. We speculate that modifications in the basal lamina are extremely significant in morphogenesis, histogenesis and cytodifferentiation.

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4.0005, INTERCELLULAR COMMUNICATION DURING TOOTH FORMATION

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During epithelial-mesenchymal interactions in numerous epidermal organ systems, there is an assumed transfer of differentiative signals between tissues. This transfer has been indirectly confirmed by heterotypic cell recombination experiments, transfilter experiments and the diffusion of various isotopic precursors from one tissue to the other in vivo and in vitro. A variety of complex embryonic organs consist of epithelial and mesenchymal components and in general, mesenchymal cells have been found to 'direct' the differentiation of epithelial components. Thus, a system has been defined which appears to rely on inductive influences from one cell to another with the concomitant differentiation of the second cell.

Several important questions arising from these observations concern the nature, reception and translation of the inducing agent or signal. Recent observations suggest that the mechanisms of induction may be mediated at the plasma membrane; and for this reason, the focus of our proposed research concerns detailed investigations of membrane events. We propose to investigate cell surface events of induction by carrying out tissue recombination and induction experiments using embryonic tooth organs in our newly-developed culture system. Specifically, we will: (1) study the nature of the mesenchymal stimulus which signals epithelial differentiation; (2) investigate the transmission of the signal at the epithelial cell plasma membrane; (3) study the contribution of selective proteolysis to inductional events; (4) study the hormonal regulation of mesenchymal-epithelial interactions; and (5) introduce experiments involving recombination of heterologous tissues derived from normal and mutant mice which show abnormalities in the development of epidermal organs including teeth.

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4.0006, MORPHOGENETIC ROLE OF GLYCOSAMINOGLYCANS

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Studies of hyaluronate metabolism in developing and regenerating tissues, and of the effect of this polysaccharide on chondrogenesis in vitro have led to an hypothesis that it prevents aggregation of mesenchymal cells, thus facilitating migration and delaying differentiation until its inhibitor effect is reversed and the molecule is removed by hyaluronidase action.

To probe the biochemical basis of this inhibition by hyaluronate and to investigate the control of its effect, we will study (1) the binding to and interaction of hyaluronate with cell surfaces; (2) the effect of hyaluronate on cell differentiation, proliferation and movement; (3) the control of hyaluronate synthesis and degradation in vitro and vivo.

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National Inst. of Dental
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4.0007, DNA-CHROMOSOMAL PROTEIN IN CRANIOFACIAL DEVELOPMENT

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The objective of our research proposal is to study the interaction of nonhistone chromosomal proteins (NHCP) with DNA/histone complexes and to chromatin. This involves the isolation of various NHCP fractions and the close examination of their binding to complexes of DNA/histones from urea-buffers. The complexes are later transcribed with homologous RNA polymerase B(II), and the RNA transcript analyzed for base sequence homology to in vivo poly A-messenger RNA, using the methods of kinetic-complexity analysis to generate a Crot curve by hybridization of RNA to cDNA. The cDNA is synthesized from poly A-mRNA isolated from mouse Ehrlich Ascites cells using RNA-dependent DNA polymerase from avian myeloblastosis virus. Through such methods we can carry out analysis on the base sequences of the RNA being transcribed. In addition, we also examine which fraction of NHCP can be linked to synthesis of tissue-specific RNA's. Our methods entail: (1) the isolation of chromatin from mouse Ehrlich ascites cells; (2) isolation of RNA polymerase from Ehrlich ascites cells; (3) fractionation of NHCP; (4) preparation of various DNA/chromosomal protein complexes; and (5) transcription. These types of experimentations will aid in determining the participation of nonhistones in the process of craniofacial development both in normal and malformed mouse embryos.

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Research $0

4.0008, MIGRATION AND DIFFERENTIATION OF NEURAL CREST CELLS

N.M. Le Douarin, Universite de Nantes, *1 Pl. Alexis Ricordeau, 44044 Nantes, France* (R01 DE 04257-03)

Our research concerns the migration and differentiation of the neural crest cells. We have used for this investigation a cell marking technique devised by the chief investigator of this proposal and based on structural differences between the interphase nucleus of two species of birds: the chick (Gallus gallus) and the quail (Coturnix coturnix japonica).

Special emphasis has been done this year on the origin of the endocrine cells of the gut epithelium and of the pancreas from the neural crest. According to Pearse's theory of the 'APUD-series', those cells, along with the adrenomedullary cells, and the calcitonin producing cells (C-cells) of the ultimobranchial bodies, would have a common ectodermal origin. In fact, large series of experiments allowed us to consider that the C-cells are derived from the rhombencephalon, but that the endocrine cells associated with the gut originate neither from the neural crest nor from the neurectoderm. We conclude that their origin from the endoderm is the most likely hypothesis at the present time.

The second point investigated concerns the determination of NC cells and the influences that the microenvironment exerts on their differentiation. We found that, as far at the autonomic nervous system is concerned, the biochemical differentiation of the autonomic ganglioblasts (in terms of neurotransmitter sysnthesis) depends upon environmental influences which are dictated to the cells by the mesenchyme in which they migrate.

In addition, the phenotypic expression of the autonomic ganglioblasts remains labile a certain time after their differentiation has been initiated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

4.0009, EXTRACELLULAR MATRIX AND MORPHOGENESIS IN MUTANT MICE

J.A. Weston, Oregon State Higher Education System, University of Oregon, School of Arts & Sciences, Dept. of Biology, *Johnson Hall, Eugene, Oregon* 97403 (R01 DE 04316-03)

Using a variety of histological and histochemical procedures, at the light and EM levels, we propose to test the hypothesis that some genetically determined abnormalities of neural crest development result from changes in the temporal and spatial patterns of synthesis, deposition and removal of glycosaminoglycans and other constituents (e.g. collagen(s)) of the extracellular matrix. We further propose to analyse how such extracellular matrix materials affect the morphogenetic behavior and differentiation of neural crest cells in vitro.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

4.0010, NERVE-EPITHELIUM INTERACTION IN OROFACIAL DEVELOPMENT

C.M. Mistretta, University of Michigan, Ann Arbor Campus, School of Dentistry, Dept. of Oral Biology, *Ann Arbor, Michigan* 48104 (R01 DE 04491-04)

Interactions between mammalian sensory nerves and oral epithelium will be studied during differentiation of lingual taste buds and gustatory papillae in fetal sheep. This examination of fetal nerve-epithelial interactions will provide a basis for understanding neurotrophic influences during oral-faciAl development. The inductive influence of non-taste nerves on lingual epithelium will be studied, as will the influence of taste nerves on non-lingual epithelium. Using sterile surgical procedures in fetal sheep early in gestation, cross-grafts will be made between dorsal tongue mucosa and other types of orofacial epithelia. Near the end of gestation, grafts will be dissected and microsopically examined for the presence of taste buds, taste papillae, and nerves. To determine whether taste buds that may form in grafted epithelial tissues are functional, electrophysiological recordings will be made from the innervation to grafted tissues; grafts will be stimulated with chemicals and tactile stimuli. The experiments will increase knowledge of: inductive and neurotrophic influences in the oral cavity during development: tissue healing and epithelial graft; underlying pathology of familial dysautonomia; and, taste receptor formation. This knowledge will contribute to understanding normal and abnormal craniofacial development.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$37,305

4.0011, STABILITY OF DIFFERENTIATION - CRANIOFACIAL STUDY

L.B. Taichman, State University of New York, Health Science Center at Stony Brook, School of Dentistry, Dept. of Oral Biology & Pathology, *Stony Brook, New York* 11790 (R01 DE 04511-04)

In the development of the craniofacial complex cells acquire differentiated states and transmit those states faithfully to daughter cells. This proposal seeks to explain in molecular terms the stability of differentiation in replicating cells. Two questions are posed: (A) How does chromatin replicate? (B) Can keratinocytes in culture undergo predifferentiation?

(A) Chromatin replication: We seek to learn if there is a coordinated assembly of newly synthesized and preexisting chromosomal proteins that might explain how the DNA-protein complexes in parental chromatin are faithfully reproduced in daughter chromatin. The experiments utilize chromatin isolation and fractionation techniques developed by the principal investigator. Four areas related to chromatin replication are explored: 1) the structure of nascent chromatin; 2) chromatin made in the absence of protein synthesis; 3) 'repaired' chromatin (i.e., following damage to the DNA by known mutagens and carcinogens); and 4) chromatin synthesized when DNA is crosslinked to chromosomal proteins.

(B) Keratinocyte redifferentiation: Single keratinocytes from oral mucosa have been cultured in vitro by the principal investigator and observed to form colonies of cells that resemble non-keratinizing stratified squamous epithelium. The stability of their differentiation is probed by culturing these keratinocytes with fibroblasts from keratinizing and non-keratinizing tissue and with agents known to block differentiation, i.e., bromodeoxyuridine. In addition, keratinocytes from oral dysplastic lesions will be cultured to learn if an altered state of differentiation is expressed in culture.

The information derived from this study will help explain how permanent phenotypic changes could arise by epigenetic mechanisms and why dysmorphogenic syndromes and neoplasia might be the pathological counterpart of normal differentiation.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$63,110

4.0012, IN VITRO ANALYSIS OF DEVELOPING ORAL-FACIAL TISSUES

W.E. Koch, University of North Carolina, Chapel Hill Campus, School of Medicine, Dept. of Anatomy, *Manning Dr., Chapel Hill, North Carolina* 27514 (R01 DE 04580-03)

Several general developmental problems using potential oral-facial tissues are under study:

The development of organized structural connective tissues of the mandibular arch of the embryo are under study using in vitro procedures. Particular differentiation of bone and cartilage.

The capabilities for differentiation of arch tissues are studied by growth of the siolated tissues from embryos of different age. These studies seek to determine the earliest embryonic age at which mandibular arch tissues are able to differentiate independently of other tissues.

Heterologous tissue recombinations are planned with the goal of understanding the developmental interrelationships between the arch tissues.

Scanning electron microscopic studies are utilized to observe the surfaces of the cells and tissues prior to and following their differentiation and to correlate the appearance of the cells with the known developmental dissimilarities between the different portions of the arch.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$82,235

4.0013, MATRIX-MEDIATED EXPRESSION IN CRANIOFACIAL EMBRYOLOGY

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The overall objective is to test whether an alteration in the molecular composition or molecular ordering of extracellular macromolecules (ECM) constitutes a principal underlying factor predisposing an embryo to defects in craniofacial (CF) development. The problem analysis focuses on the neural crest progenitor of CF tissue and asks the following questions: (1) What is the chemical nature of the abundant amorphous extracellular material which surrounds migrating cephalic neural crest cells and CF primordia? (2) Does any particular spatial ordering (molecular packaging) of the matrical substances impart instructive or regulatory information on cephalic neural crest migration or determination? (3) Do any of the extracellular substances (individually or in combination) have direct inductive influences on the phenotypic transformation of cephalic neural crest into the mesenchymal derivatives of CF primordia? In both chick and rat embryos, identification and distribution of ECM (correlated to the movement of migrating crest cells) will be based on transmission and scanning EM analyses of fixed or carbon platinum replicas of frozen-dried cephalic primordia exposed to specific enzymic or extractive techniques and alcian blue, lectin, dialyzed iron, or immunocytochemical staining or x-ray detection of sulfur emission matrix inhibitors (Diazo-5 oxo-L-Norleucine for glycosaminoglycans and azetidine for collagen) together with lysozyme and Beta-aminoproprionitrile will be used to evaluate the significance of molecular ordering (the latter two agents disrupt inter-molecular associations without directly affecting short term cell synthesis). Individual compositional contributions of the various matrical macromolecules to the morphogenesis of CF primordia will be tested in two and three dimensional tissues of normal plate or cephalic mesenchyme explants. Individual moieties or combinations of varying ratios of matrix moieties will be added for the culture medium or incorporated into substrates on which the cells are grown. Data should indicate if matrix organization and composition are directly related to CF development and if microenvironmental alterations in CF constitute molecular pathway of abnormal CF development.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$38,899

4.0014, MATRIX-CELL INTERACTION IN CRANIOFACIAL DEVELOPMENT

S.P. Meier, University of Southern California, School of Medicine, Dept. of Anatomy, *2025 Zonal Ave., Los Angeles, California* 90033 (R01 DE 04613-02)

From the results of new ultrastructural observations it is likely that chick otic placode formation is not the result of contact of epithelial and neural crest cells in the sense of membrane to membrane apposition. Even though neural crest cells don't actually contact placode cells, their precisional time of appearance and location make it likely that they are interacting. The most obvious change which occurs between them is the buildup of ECM which is very collagenous. Experiments which are underway include: 1) an autoradiographic analysis of the source of various ECM components found in the tissue interspace, 2) the influence of this matrix on placode and neural crest cell differentiation, and 3) the effect of selective enzymatic removal of ECM components on otic development. Since the assay for placode formation is restricted pseudostratification and invagination, the influence of ECM on these processes will be analyzed as well. Ultrastructural analyses continue along several lines. The process of neural crest formation from rhombencephalon is to be examined at the transmission and stero scanning electron microscopic level. Other craniofacial 'mesenchymalizations' from epithelium--including sclerotome formation from somite, epibranchial placode cell contributions to cranial ganglia, and otic placode cell exit from otocyst--are being examined for comparison.

BIBLIOGRAPHIC REFERENCES: Meier, S. 1978. Development of the embryonic chick otic placode. I. Light Microscopic Analysis. Anat. Rec. (in press). Meier, S. 1978. Development of the embryonic chick otic placode. II. Electron Microscopic Analysis. Anat. Rec. (in press).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

4.0015, CHARACTERIZATION OF SYMPATHETIC NEURON DIFFERENTIATION

S.C. Norr, Georgetown University, School of Arts & Sciences, Dept. of Biology, *3800 Reservoir Rd. N.W., Washington, District of Columbia* 20007 (R01 DE 05057-01)

Neural crest cells differentiate into sympathetic neurons and other cell types in response to specific tissue interactions or their environmental stimuli. Preliminary evidence suggests that these interactions might be mediated by one or more extracellular matrix (ECM) materials. Neural crest cells contribute extensively to connective tissues, glandular and neuronal elements of the head. Therefore, a study of ECM influence on neural crest cell differentiation is useful to the understanding of craniofacial development in addition to neuronal development.

Chick neural crest cells require a specific sequence of interactions with ventral neural tube and somite tissue in order to differentiate in organ culture into sympathetic neurons, detectable by specific formaldehyde-induced fluorescence assay for catecholamines. The proposed research is designed to further characterize these interactions: 1) fluorescent cells, which appear in organ culture, will be classified, by histological and diagnostic procedures, as prinicpal neurons or small intensely fluorescent (SIF) cells. 2) The timing of the competence of the various tissues in the organ culture system to support sympathetic neuron differentiation will be determined. 3) The relationship between ECM and sympathetic neuron differentiation in the organ culture system will be examined by using enzymes and other chemicals to interrupt or promote cartilage matrix formation. 4) A neural crest culture system will be developed which supports sympathetic neuron differentiation. This system will involve the deposition of ECM in a Millipore filter by cultured neural tube plus somite. 5) The ECM residues in the treated filters will be analyzed for glycosaminoglycans and collagen. 6) Various ECM's, hormones, growth factors, and neural crest cell interactions will be examined for effects on sympathetic neuron differentiation. 7) Cell culture conditions will be developed which will support growth of neural crest cells and then their differentiation into sympathetic neurons only in response to a regulated environmental stimulus.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $51,858

4.0016. MATRIX-CELL INTERACTION IN CRANIOFACIAL DEVELOPMENT

S.P. Meier, University of Texas, Austin Campus, School of Natural Sciences, Dept. of Zoology, *200 W. 21st St., Austin, Texas* 78712 (R01 DE 05616-01)

In the period for which funding is sought, I plan to study the role of extracellular matrix (ECM) in embryonic induction of craniofacial tissues. This work includes an extensive ultrastructural analysis of embryonic placode formation, comparing the development of optic, otic, and nasal anlage by scanning and transmission electron microscopy. The extracellular matrix components associated with the development of these placodes will be biochemically characterized and the relation of surface components to intracellular organelles clarified. Using the interaction between the lens epithelium and neural retina as a model system, the influence of the lens placode-neural epithelium ECM interface on the establishment and maintenance of placode morphology will be studied in vitro. Likewise, the influence of the ECM interface on subsequent invagination of the lens analage will be evaluated. In addition, I will analyze the role of the lens anlage interface ECM on the production lens fibers and proteins by the invaginated lens epithelium. Other relatively undifferentiated embryonic epithelia will be challenged with lens-neural epithelium interface ECM to produce a placode, invaginate, and/or synthesize lens fibers. Experiments on the otic and nasal placodes will be designed using this basic information derived from study of lens induction. Finally, I will extend our recent studies on the role of ECM in the development of the cornea. Corneal epithelium of earlier stages than heretofore employed will be combined in vitro with lens or eye cup to determine the extent to which these tissues and their ECM influence the presumptive corneal epithelium to begin producing a primary stroma. The degreee to which other relatively uncommitted epithelia can respond to corneal 'inductors' will also be assessed by tissue combination in vitro. Clarification of the role of ECM in embryonic tissue interaction will provide information leading to our understanding of normal and abnormal development of craniofacial structures.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $43,282

4.0017. CELL-MATRIX INTERACTIONS

R.W. Orkin, Massachusetts General Hospital, Dept. of Medicine, *32 Fruit St., Boston, Massachusetts* 02114 (R23 DE 04734-03)

The main objective of this research is to study further the biochemical interactions occurring between specific macromolecules which comprise extracellular matrices. These macromolecules include proteoglycans, gycosaminoglycans, collagens and glycoproteins, including fibronectin (also known as LETS: large, external, transformation sensitive glycoprotein). An additional aspect of this study includes an examination of the effects of these macromolecules on cell behavior, especially during morphogenesis and tissue remodelling.

During the coming year we will extend our studies with respect to the interactions occurring 1. between basement membrane-type collagens and proteoglycans, 2. between collagen proteoglycan interactions in the developing limb bud, and 3. possible role of fibronectin in regulating collagen-proteoglycan interactions and its effect on matrix deposition. We will continue our studies on the effects of defined substrates on cell behavior, using chondrogenesis as a model system. The latter studies will be extended to monitor biochemically the synthesis of collagen and proteoglycan species in micromass cultures, established from young chick embryo limb buds and grown on known substrates. We will also examine further the relationships of fibronectin to chondrogenesis and matrix deposition in this system.

These studies have direct bearing on heritable and congenital disorders of connective tissue and disorders resulting from the synthesis of abnormal extracellular matrix material during tissue remodeling.

BIBLIOGRAPHIC REFERENCES: Orkin, R.W. and B.P. Toole. 1978. Hyaluronidase activity and hyaluronate content of the developing chick embryo heart. Dev. Biol. 66, 308-320.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $28,482

4.0018, TISSUE INTERACTIONS IN THE CRANIOFACIAL REGION

M.S. Tyler, University of Maine, Orono Campus, School of Arts & Sciences, Dept. of Zoology, *36 Winslow Hall, Orono, Maine* 04473 (R23 DE 04859-02)

The major objective of this research project is to further elucidate the function of tissue interactions during morphogenesis and histogenesis of organ systems within the cranio-facial region. Ultrastructural studies in combination with light-microscopic studies are being made to reveal the developmental sequence of tissue differentiation, and experimental in vitro studies are being made to determine the flexibility and the precise requirements of differentiating tissues within the cranio-facial region. The specific aims of the project are the following: 1) A detailed study of membrane bone formation within the cranio-facial region is being made (using primarily the membrane bones of the mandibular, maxillary, and palatal (regions) in order to determine the influence of epithelium membrane bone formation. 2) A detailed study of morphogensis and histogenesis of epithelia from various oral-facial organs (palate, salivary gland, tongue, tooth) is being made to determine more precisely the factors which control the parameters of epithelial differentiation and the role that mesenchyme and extracellular matrices play in directing and influencing epithelial histogenesis and morphogenesis.

BIBLIOGRAPHIC REFERENCES: Tyler, M.S., and R.M. Pratt, 1979. Effect of epidermal growth factor on the isolated palatal epithelium in vitro. J. Dent. Res., (in press). (Abstract) Tyler, M.S., 1978. Epithelial influences on membrane bone formation in the maxilla of the embryonic chick. Anat. Rec., 192: 225-234.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$26,449

4.0019, TISSUE INTERACTIONS DURING ODONTOGENESIS

D.L. Hasty, University of Tennessee, Center for the Health Sciences, School of Basic Medical Sciences, Dept. of Anatomy, *800 Madison Ave., Memphis, Tennessee* 38163 (R23 DE 05062-01)

This proposal will concentrate on the study of the mechanisms of interaction of heterologous tissues during odontogenesis. The specific aims can be summarized as follows: A. Experimental recombinations of epithelial and mesenchymal components of dental and non-dental embryonic tissues will be used to isolate and define specific populations of odontogenic cells. Any tissues capable of interacting to form tooth-like structures can be considered odontogenic. Differences in odontogenic and non-odontogenic tissues will be characterized using biochemical and ultrastructural techniques. B. The interaction of odontogenic tissues with natural (micro-dissected tooth matrix) and artificial (collagen/GAG) gels) collagenous matrices will be used to study the effect of specific extracellular matrix (ECM) macromolecules on cellular function and cytodifferentiation. C. Biochemical techniques (CM-cellulose chromatography of collagen chains and CNBr peptides and specific polysaccharidase assay of GAG) will be used to characterize the ECM macromolecules produced during odontogenesis in vivo and in vitro. If the ECM is found to affect the differentiation of ameloblasts or odontoblasts, it will be important to know the specific components of that matrix. D. Ultrastructural techniques, such as freeze-fracture and histochemistry, will be used to further characterize the ECM and the plasmalemma and cell surface of odontogenic and non-odontogenic cells. The information obtained will be used to evaluate the relative roles of cell-ECM and cell-cell interactions in organogenetic tissue interactions.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$28,700

4.0020, CHEMISTRY AND BIOSYNTHESIS OF CONNECTIVE TISSUE

G.R. Martin, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00009-18 DB)

For summary: see 7.0005.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$54,970

4.0021, CELLULAR PROLIFERATION AND DIFFERENTIATION DURING CRANIOFACIAL DEVELOPMENT

R.M. Pratt, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Craniofacial Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00149-05 DB)

The long range purpose of this project is to understand the regulation of cellular proliferation and differentiation in craniofacial tissues. At present we are 1) developing an in vitro method for screening teratogens; 2) developing methods to culture craniofacial tissues; 3) determining the biochemical events that regulate palatal development; and 4) determining the biochemical events in odontoblast differentiation and incisor tooth eruption.

BIBLIOGRAPHIC REFERENCES: Figueroa, A. A. and Pratt, R.M.: Autoradiographic study of macromolecular synthesis in the developing rat primary palate in vitro. J. Embry. Exp. Morph. 50: 145-154, 1979. Greene, R. M. and Pratt, R.M.: Correlation between cyclic AMP levels and cytochemical localization of adenylate cyclase during development of the secondary palate. J. Histochem. Cytochem. 27: 924-931, 1979.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $309,503

4.0022, COLLAGENOUS MATRIX AND BONE DIFFERENTIATION

A.H. Reddi, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Molecular Structure Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00204-03 LBS)

For summary: see 2.0228.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $51,787

4.0023, DEVELOPMENT OF CARTILAGE

J.P. Pennypacker, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00253-02 DB)

The factors influencing chondrogenesis are under study. Particular attention is being directed towards the extracellular matrix of developing cartilage and its relationsip to normal cellular function. In these investigations, use is being made of limb mesenchyme cell cultures, mature chondrocytes in culture, cartilage producing tumors and cartilage from various animal mutants which may serve as models for human chondrodystrophies.

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SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $151,571

4.0024, DIFFERENTITION OF CRANIAL NEURAL CREST CELLS

J.H. Greenberg, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Craniofacial Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00257-01 DB)

Cranial neural crest cells, which contribute to the formation of many craniofacal structures, differentiate in culture into two of their normal derivatives, neurons and pigment cells. As an approach toward defining the factors which affect normal and abnormal neural crest development, we are examining various aspects of their differentiation in culture. The well-defined and reproducible differentiation of neural crest cultures has enabled us to develop a system to screen for teratogens in vitro.

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Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $110,670

IV. CRANIOFACIAL ANOMALIES, GENERAL

4.0025, CELLULAR ASSEMBLY - ITS ROLE IN FACIAL MORPHOGENESIS

E.F. Rossomando, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Oral Biology, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 03715-05)

The purpose of this proposal is to better understand the mechanism underlying the process of multicellular assembly exhibited by cranial neural crest cells during facial morphogenesis. It is proposed that this process occurs by a self-assembly mechanism. To test this hypothesis, the eukaryotic microorganism Dictyostelium discoideum was chosen for study. This organism forms a multicellular aggregate from genetically, biochemically and cytologically identical cells at a specific stage in its development. Since these cells assemble by a signalling system involving cAMP, the possibility exists that this system is the mechanism regulating assembly.

To better understand this signalling system, experiments on the D. discoideum adenylate cyclase are described. Experiments are planned to explore the mechanism underlying the ATP induced loss of catalytic activity. One enzymatic reaction to be examined in some detail is the adenyl transfer activity. The product of the reaction is to be isolated and characterized. Further, the role of the 5'-nucleotide phosphodiesterase in the deadenylylation reaction will be studied using 4-nitrophenyl phenylphosphonate. The effect of this phosphonate ester on adenylylation product formation, AMP formation and finally on adenylate cyclase activity will also be studied. Studies on the 4-nitrophenyl phenylphosphonate activity itself will also be undertaken. These include isolation and purification of the enzyme and its developmental regulation.

BIBLIOGRAPHIC REFERENCES: Crean, E.V. and Rossomando, E.F. 1977. Developmental changes in membrane-bound enzymes of Dictyostelium discoideum detected by Concanavalin A- sepharose affinity chromatography. Biochem. Biophys. Res. Comm. 75: 488-495. Rossomando, E.F., Hesla, M.A., Heitz, M.A. and Maldonado, B. 1977. Aggregation-dependent changes in sensitivity of Dictyostelium discoideum to Amphotericin B. Antimicrob. Agents and Chemotherapy. 11: 858-864

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$38,715

4.0026, ABNORMAL PALATAL DEVELOPMENT INDUCED BY HADACIDIN

E.F. Rossomando, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Oral Biology, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 04657-03)

One stage in the palatal fusion process is epithelial autolysis. One objective of this proposal is to probe the mechanism underlying this event. To accomplish this, I propose to study those cellular changes brought about by the drug hadacidin. Previous studies have shown that this teratogen blocks the de novo synthesis of AMP by inhibiting the enzyme adenylosuccinate synthetase. We have shown that the eukaryotic microorganism Dictyostelium discoideum contains this enzymic activity and that its level declines with the onset of cellular differentiation. Further we have shown that hadacidin also causes changes to certain physiological functions such as osmotic stability and nutrient transport. We plan to continue our investigations on the effects of hadacidin on properties of the cell surface. We also plan to follow the fate of hadacidin after it is taken up by the cells as well as to purify further the adenylosuccinate synthetase of this organism.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$41,094

ETIOLOGY - GENETICS

4.0027, HUMAN GENETICS

C. Kaye, University of Illinois, Medical Center at Chicago, Abraham Lincoln School of Medicine, Dept. of Pediatrics, *1853 W. Polk St., Box 6998, Chicago, Illinois* 60680 (P01 DE 02872-100055)

Studies in clinical genetics fall into several broad categories: (a) identification and analysis of specific patients with rare syndromes; (b) family studies in 204 families with microtia, with or without other anomalies; (c) studies in congenital palatopharyngeal incompetence.

Review of findings in the microtia study reveals that these group of disorders (hemifacial microsomia, Goldenhar syndrome, oculoauriculovertebral syndrome, microtia) probably represent a single disorder, or continuation of severity, inherited in the multifactorial mode. Complete study of first degree relatives, followed by segregation analysis, is planned.

The CPI project is currently in the stage of (1) complete description of patients with development of an appropriate classification system; and (2) collection of complete pedigrees. In the near future, pedigree analysis will be begun and complete family studies will be initiated.

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Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $16,637

4.0028, CRANIOFACIAL ANOMALIES - ETIOLOGY AND TREATMENT (GENETICS)

J.M. Converse, New York University, School of Medicine, Dept. of Surgery, *550 1st Ave., New York, New York* 10016 (P01 DE 03568-050007)

A series of studies have been designed to test possible relationships between the HL-A complex and the occurrence of craniofacial anomalies within the patient population under investigation at the Center for Craniofacial Anomalies. For this purpose, each afflicted individual, his or her parents and one or more normal siblings underwent complete HL-A (SD) and (LD) studies, and an attempt was made to compare the incidence of HL-A antigens, haplotypes, and genotypes in affected siblings, normal siblings and parents. The incidence of paternal-maternal HL-A incompatibilities and of shared antigens and haplotypes was also determined, and the data were compared with the results of similar studies performed in a parallel number of normal family units. In addition, an attempt was made to trace the transmission of HL-A determinants from parents to offspring.

Within the limitations of the population sample tested thus far, no evidence has been obtained of associations between any particular HL-A antigen(s) or haplotype(s) with any particular form of craniofacial anomaly. A significant portion of the families with cleft lip-cleft palate anomalies has, however, exhibited evidence of atypical inheritance of HL-A (SD) antigens, including instances of antigen gains or losses by the offspring, which may constitute unequal cross-over events. In addition, 18 of 56 families included in this study provided evidence of sharing of LD alleles by the parents. This sharing of LD determinants was not related to paternal-maternal states of compatibility for HL-A A or B (SD) determinants.

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National Inst. of Dental
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IV. CRANIOFACIAL ANOMALIES, GENERAL

4.0029, ORAL-FACIAL GROWTH AND DEVELOPMENT IN PRIMATES

O.A. Smith, University of Washington, Regional Primate Research Center, Dept. of Physiology & Biophysics, *c/o Health Sciences Ctr., Seattle, Washington* 98195 (R01 DE 02918-10)

This project focuses on prenatal and postnatal growth and development of the oral-facial complex. Major objectives are (1) to investigate the growth and development patterns of the prenatal and neonatal Macaca nemestrina; (2) to define the prenatal and neonatal chronological-structural relationship of tooth development and to assess its role in oral-facial growth and development; and (3) to describe and quantify the patterns of normal prenatal and neonatal growth and development in the craniofacial complex.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

4.0030, DEVELOPMENTAL PROCESSES IN GENETICALLY CONTROLLED MALFORMATIONS

K.S. Brown, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00024-13 DB)

The objectives of this project are to describe the genetic mechanisms and developmental processes in mutant and highly inbred animals with hereditary predisposition to congenital malformations, particularly involving the face and limbs, and to utilize these animals as experimental systems for the study of the processes of congenital malformation. Mouse strains with hereditary malformations as Mendelian or non-Mendelian traits have been discovered in this laboratory or are obtained from others. Comparison of normal and abnormal development are carried out in embryos of timed gestational age using gross examination of living embryos, whole mount preparations and histological sections as well as biochemical analyses of tissues and or cultured organs and cells. Genetic analysis involves segregration analysis, selection of sublines, cross breeding of abnormal and normal lines and genetic linkage studies. Agents such as drugs, vitamins and hormones are used as probes for the study of gene action in hereditary malformations and for the study of possible human teratogens.

IV. CRANIOFACIAL ANOMALIES, GENERAL

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$110,690

4.0031, CHROMOSOME DAMAGE FROM RADIATION AND CHEMOTHERAPY

C.E. Nasjleti, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *2215 Fuller Rd., Ann Arbor, Michigan* 48105 (506-002-P)

This long-term investigation is progressing according to plans. As a by-product of this research, we recently published.

The location of the Y chromosome in metaphase spreads is studied in groups of (a) 96 normal males, (b) 17 Down's syndrome patients, and (c) 15 patients with Klinefelter's syndrome. The position of the Y is scored as either peripheral or nonperipheral using several of the traditional definitions found in the literature. It is shown that contradictory results may be obtained depending on the particular definition employed and that none of the available definitions capture the essence of the meaning of 'peripheral'. Therefore a new, standardized definition is introduced--one that applies to both circular and noncircular spreads. Using this new definition, we find definite intergroup variability. The Y is peripheral in normal males, but not in either the Down's or Klinefelter's samples.

Another paper entitled 'The length of the Y chromosome in Nubian males and its location in metaphase spreads' is in press, Journal of Human Genetics.

BIBLIOGRAPHIC REFERENCES: On the Peripheral Location of the Y Chromosome by Kowalski, C.J., Nasjleti, C.E. and Schmitt, B.: Human Genet., 44, 123-135, 1978.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

4.0032, ODONTOGENESIS - A GENETIC STUDY OF AMELO AND DENTINOGENESIS IMPERFECTA

J.P. Gage, University of Queensland, Cytogenetics Lab., Dept. of Biochemistry, *St. Lucia, Brisbane, Queensland 4067, Australia*

AMELOGENESIS IMPERFECTA: Cytogenetic Pedigree and Linkage studies on known Amelogenesis Imperfecta patients with particular reference to known marker genes on the X-chromosomes and linkage studies with known markers on some of the autosomes, in particular chromosome 9, in order to ascertain genetic control of amelogenesis.

DENTINOGENESIS IMPERFECTA: Extraction of collagen from the dentine of exfoliated and extracted D/I teeth in order to carry out amino acid analysis of the alpha chains. Should sequence or quantity of a particular amino acid be altered, then further studies with cell hybridization of human cells (fibroblasts, lymphocytes) with auxotrophic hamster/mouse cells will be carried out in an effort to elucidate chromosome(s) responsible for synthesis of the particular amino acid.

SUPPORTED BY

University of Queensland	funds n.a.

ETIOLOGY - EMBRYOLOGY

4.0033, PALATAL NEURAL CREST AND EFFECT OF TERATOGENS (MICE)

E.F. Zimmerman, Childrens Hospital Medical Center, *3245 Burnet Ave., Cincinnati, Ohio* 45229 (P01 HD 12285-010001)

This project is part of a broader program (HD 12285-01) whose summary states: The causes of most human mental retardation and neurological defects remain unknown. We propose to use teratological, biochemical, and immunological approaches to determine whether defects in selected molecular and cellular components result in gross abnormalities of the nervous system and related tissues. An evaluation will be made of the role of contractile elements (actin, myosin and related proteins) in motile processes essential to normal neural development. Antibodies to these components will be used in efforts to experimentally produce neural defects in chicks and mice. Likewise, the role of specific neural cell surface antigens in brain organogenesis will be examined and efforts to experimentally induce neural defects with antibodies to these components initiated. Human amniotic fluid and serum samples will be tested for antibodies to cytoskeletal proteins and neural specific cell surface antigens. In another approach, the presence and role of neural crest cells in the morphogenetic movement of mouse palate will be examined. Factors influencing the migration of neural crest cells will be tested. The effects of chemical teratogens on cultured neural crest and non-neural cells will be examined to determine if neural cells are particularly sensitive to these agents. The combined analysis of these molecular and cellular aspects of neural development should lead to more rational approaches to the etiologies of human mental retardation.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,

National Inst. of Health,
National Inst. of Child Health
& Human Development funds n.a.

4.0034, NORMAL AND ABNORMAL EMBRYONIC FACIAL DEVELOPMENT

M.C. Johnston, University of North Carolina, Chapel Hill Campus, Dental Research Center, Dept. of Orthodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130172)

For summary: see 5.0010.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $52,016

4.0035, ROLE OF VASCULARIZATION DURING CRANIOFACIAL DEVELOPMENT

N. Sorgente, University of Southern California, School of Dentistry, Dept. of Ophthalmology, *3551 University Ave., Los Angeles, California* 90007 (R01 DE 04074-05)

During development the proper spacial and temporal development of the vasculature is of fundamental importance to normal morphogenesis. During craniofacial development, aberrant vasculature has been suggested to be causally related in the etiology of a number of congenital anomalies (Poswillo, 1975; Gregg and Avery, 1971). Does the vasculature furnish developmental cues which modulate or are permissive to cell differentiation during organogenesis? Using cortisone acetate and triamcinolone acetate to treat A/Jax mice and chick embryos to produce craniofacial anomalies we will investigate the patterns and the functionality (permeability, ionic composition of blood, integrity of the capillaires) of the developing vasculature and determine the relation of the vasculature to organogenesis will be examined using the chick chorioallantoic membrane grafting technique for explanting tissues, as a bioassay for the differentiation and morphogenesis of the limb and the formation of endochondral bone in a vascular and avascular environment. Inhibitors of vascular gorwth, which are present in cartilage and avascular tissue, will be purified and their effect on endothelial cell proliferation and metabolism will be investigated. These studies will provide an understanding of the role of the vasculature in development, and its relation to craniofacial anomalies. They will also provide an insight into the mechanisms of cell-cell interaction and communication related to the development of the vasculature vis-a-vis organogenesis. These investigations are an imperative prerequisite to the understanding and prevention of craniofacial anomalies.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $88,646

4.0036, ADAPTIVE GROWTH POTENTIAL OF EMBRYONIC CARTILAGE

J.D. Heeley, Forsyth Dental Center, Histology & Histochemistry, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 04236-03)

Previous work in the Department of Histology and Histochemistry has been concerned with the tibial growth plate, tibial articular and mandibular condylar cartilages. Observations of the histochemistry, histomorphology and growth patterns of these sites as well as their responses to some nutritional upsets have led to our belief that the condylar and articular cartilages are 'embryonic' in structure and exhibit an 'adaptive growth potential' unlike the growth plate which is a 'primary growth center.'

Our prime research objective is to further clarify the 'adaptive growth potential' of the cartilage of the mandibular condyle, the nasal septum, and that of the tibial articular cartilage. In vitro organ culture techniques, histological, histochemical and radioautographic observations will be utilized. If these methods substantiate the hypothesis that adaptive growth can occur when the sites are in a 'hypertrophic form' but can not occur when the cartilages are 'non-hypertrophic' we would attempt surgical transplantation in laboratory animals in an effort to mirror current surgical approaches to correcting some cranio-facial anomalies involving the mandibular condyle. Mechanisms of cartilage erosion will also be studied. Chondroclasts will be studied utilizing histochemical, autoradiographic and electron microscopic techniques to attempt to determine their origin and mechanism of erosion. These same tools will be employed to study capillary erosion in a primary growth cartilage, the tibial epiphysis growth plate.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $58,086

IV. CRANIOFACIAL ANOMALIES, GENERAL

4.0037, QUAIL CELL GRAFTS AND THE CHICK TRIGEMINAL GANGLION

G.C. Gaik, Loyola University of Chicago, Maywood Campus, School of Dentistry, Dept. of Anatomy, *Maywood, Illinois* 60153 (R01 DE 04785-02)

The cellular changes associated with the development and maturation of the chick trigeminal ganglion can be summarized as follows: (1) dual cellular origin from neural crest and placodal ectoderm material; (2) transitory topograhical arrangement of small- and large-sized cells; (3) an apparently random distribution of small and large neurons; and (4) final random arrangement of dark and light neurons. Although it has been demonstrated that the neural crest cells were the precursors of the small cells and that the placodal ectoderm cells were the precursors of the large cells, no such correlation has been investigated concerning the dark and light trigeminal neurons.

It is the specific aim of this work to investigate the relationship between the topographically arranged small and large cells within early developing chick trigeminal ganglia and the dark and light neurons observed within post-hatching and adult ganglia. Due to differences in nuclear morphology, the quail cell is quite easily distinguished from the chicken cell. Isotopic and isochronic grafts of both quail neural crest material and placodal ectoderm material will be orthotopically placed into chick embryos of the same age. Chorioallantoic membrane grafts and the horseradish peroxidase retrograde tracer technique will also be used to further define this relationship. In this manner, the migration of the quail cells and their fate in relation to small and large cells and dark and light cells can be investigated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$4,400

4.0038, VISCERAL ARCHES AND ORO-FACIAL MORPHOGENESIS

A. Tamarin, University of Washington, School of Dentistry, Dept. of Oral Biology, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (R01 DE 05138-01)

This research project is addressed to the question of how the visceral arches develop and how they contribute to the morphogenesis of the oro-facial complex. A basic aspect of the approach to this question is to compare and contrast the development of the embryonic landscape in the mouse and in an infrahuman primate under laboratory conditions wherein development time and specimen preparation are strictly controlled. Scanning electron microscopy with microscopy will provide surface and subsurface details of changing contours and cell differentiation. Growth equations and photogrammetric analysis in three dimensions will be used to analyze changes with time and to show differences between species at comparable stages of embryonic development.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$52,785

ETIOLOGY - CRANIOFACIAL GROWTH

4.0039, CRANIAL GROWTH DEVELOPMENT (SUB-PROJECT C) ANALYSIS OF CRANIOFACIAL SHAPE CHANGE AND ORAL DEVELOPMENT

R.E. Moyers, University of Michigan, Ann Arbor Campus, Center for Human Growth & Development, *Ann Arbor, Michigan* 48104 (P01 DE 03610-130016)

Morphometrics for three dimensional data: After scrutiny of several other studies of three-dimensional form, we have concluded that the most practical representation system is by way of three-dimensional medial surfaces, and are currently expanding the computational geometry from two dimensions to three.

Medial Axes: A new algorithm has been invented for easier extraction of the axes from high-order polygons, such as those we have archived. This procedure has been programmed for routine application to manibular outlines and other geometric data sets.

Craniofacial Growth Analysis: We have applied the biorthogonal method to treatment assessment of severe craniofacial anomalies. Also, the measurement of pairs of form has been extended to series of three, so that in our studies of prediction we may sort out aspects of persistent vs. transient form changes. Identification of persistent aspects of form (pattern) has successfully segregated facial types within the clinical group called angle Class II malocclusions and are now studying the effects of orthodontic treatment on each type.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$69,185

4.0040, CRANIOFACIAL GROWTH AND DEVELOPMENT (SUB-PROJECT B) CRANIOFACIAL PROFILE PATTERNS IN NORMAL INDIVIDUALS, FETUSES AND IN MALFORMATION SYNDROMES

A.R. Burdi, University of Michigan, Ann Arbor Campus, Center for Human Growth & Development, *Ann Arbor, Michigan* 48104 (P01 DE 03610-130017)

This research is concerned with (1) changing shape and size patterns of the human craniofacial region as related to age, race, sex, familial and clinical histories in representative populations of human prenates, postnates and congenital malformation syndrome types; and (2) the graphic display of pattern information.

Preliminary work confirms a linear increase in width in prenates for various sex and race groups, corraborating existing reports which had not referenced the Specific race, sex and familial histories. Our data go further and support the hypothesis that there are sex and race pattern differences in the prenatal period of humans which should be used whenever assessing growth status.

Postnatally, our studies on dental asymmetry show that many reported differences in crown size asymmetry may be a function of sample size. We have also shown that the pattern of developmental asymmetry is the same in the maxilla as in the mandible. We have studied maxillo-mandibular precedence and mesio-distal sequence relating sequence differences within the arches to precedence relations between the arches.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$71,197

4.0041, CRANIOFACIAL GROWTH AND DEVELOPMENT (SUB-PROJECT A) EXPERIMENTAL STUDIES OF THE FUNCTION AND GROWTH OF THE TEMPOROMANDIBULAR JOINT

J.A. McNamara, University of Michigan, Ann Arbor Campus, Center for Human Growth & Development, *Ann Arbor, Michigan* 48104 (P01 DE 03610-130018)

Our objective is to determine the effects of neuromuscular activity and biomechanical forces on the growth of the temporamandibular joint using growing rhesus monkeys as experimental models. A long term cephalometric experimental study of growing rhesus monkeys in whom we have placed functional protrusion appliances continues using 6 female monkeys over two years into the experiment and three over one year. Histologic analysis of temporomandibular growth following functional protrusion has been reported. We found that condylar cartilage growth increased through the six weeks of the experiment and then subsided to within control limits. Long term analysis of monkeys who have undergone bilateral lateral pterygoid myectomy is continuing using cephalometry and histology.

This research on factors which influence mandibular condylar growth is important because it is directly related to the clinical treatment of mandibular deficiency in human patients.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$111,199

4.0042, THE PERIOSTEAL INTERFACE IN CRANIOFACIAL DEVELOPMENT

C.A. Evans, Harvard University, Boston Campus, School of Dentistry, Dept. of Orthodontics, *188 Longwood Ave., Boston, Massachusetts* 02115 (R01 DE 04684-03)

Factors controlling the surface growth of the mandible may operate through its membranous capsule, the periosteum. To investigate the role of periosteal attachment, tension, and migration in the growth of the membranous facial bones, the following objectives have been established for the proposed reseaach: the development of a periosteal migration map of the growing mandible; the determination of the biochemical structure of the mandibular periosteum; the study of the synthesis of macromolecules in free periosteal segments in vitro; the determination of cross linking profile differences between periosteum of young and nongrowing animals; and the description of the alterations in periosteal cell mitosis and migration patterns following manipulations in living animals. The results of these experiments in combination with an examination of sites of bone deposition and resorption and muscle attachments may elucidate how the periosteal interface receives stimuli and translates them into bone form. Such information may subsequently make it possible to alter facial growth more successfully during the treatment of craniofacial malformations and skeletal disproportions.

BIBLIOGRAPHIC REFERENCES: Evans, C.A. Development of a mandibular periosteal migration map. J. Dent. Res. 57:95, 1978. Chong, D. and Evans, C. A histochemical description of rat mandibular periosteum. J. Dent. Res. 57:170, 1978.

IV. CRANIOFACIAL ANOMALIES, GENERAL

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $48,239

4.0043, ADJUSTIVE CRANIAL SKELETAL GROWTH

M.L. Moss, Columbia University, College of Physicians & Surgeons, Dept. of Anatomy, *630 W. 168th St., New York, New York* 10032 (R01 DE 05145-01)

It is clinical commonplace that normal cephalic growth produces racial, familial and individually specific patterns of size and shape. Similarly many craniofacial malformations are characterized by syndrome specific head growth patterns. In all cases, normal and abnormal, such patterned growth can occur only by processes of adjustive cranial skeletal growth. While it is agreed that such processes must exist, no comprehensive conceptualization exists as to what these processes are or how they are regulated.

Using models both normal and experimentally produced abnormal cephalogenesis in the rat, all of which involve marked alterations in growth patterns, we propose to describe and analyze all stages of normal adjustive cranial growth, to demonstrate the processes involved and to validate these results by a similar study of the sequential compensatory changes occurring in experimentally produced cephalic deformations. This will permit creation of a general theory of adjustive cranial growth.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $52,020

4.0044, MINERALIZATION STUDIES RELATED TO ORAL BIOLOGY

H.C. Anderson, University of Kansas, Medical Center, School of Medicine, Dept. of Pathology, *39th St. & Rainbow Blvd., Kansas City, Kansas* 66103 (R01 DE 05262-02)

The proposed study will focus on enzymes of matrix vesicles which play a role in the mineralization of teeth. Matrix vesicles are submicroscopic, extracellular, membrane-invested particles which serve as the initial loci of mineralization of dentin, and of other oral tissues including cartilage and bone. Our lab was involved in the original identification of matrix vesicles and in their subsequent isolation and partial characterization. We have provided evidence that matrix vesicle phosphatases (including ATPase, pyrophosphatase and alkaline phosphatase) are involved in triggering mineralization. Furthermore, these phosphatases reside on the vesicle membrane surface and can be solubilized by deoxycholate treatment with preservation of enzymatic activity and calcium-depositing ability. Two general types of studies with the solubilized enzyme are proposed: 1) chemical purification and characterization as to molecular size, inhibitors, substrate and cofactor requirements and 2) analysis and control of calcium accumulation by vesicle phosphatase including an electron microscopic study of this process.

This is a fundamental study of the mechanism by which normal dentinal and other forms of mineralization are brought about. Techniques for tissue fractionation, radioisotopic labelling and counting, enzyme biochemistry and electron microscopy will be employed. New knowledge of matrix vesicle calcification can be applied to a broad range of topics including specific disease states in which there is abnormal calcification.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $52,090

4.0045, ANATOMICAL STUDIES OF THE HEAD

J.F. Bosma, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Oral & Pharyngeal Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00048-08 CI)

This is the eighth year of anatomical studies of the face, pharynx and cranium of the human fetus at term. The Cranium of the Newborn Human: An Atlas of Tomographic and Anatomic Sections under authorship of Robert H. Pierce, Michael W. Mainen and James F. Bosma was published by the U.S. Government Printing Office in 1977. It has been distributed to prospective reviewing journals and is on sale by the Superintendent of Documents, U.S. Government Printing Office.

A general anatomy book, The Head of the Human Infant, is in preparation of text matching the completed illustrations. Portions of the book are now in critical review.

A collaborative contract project with Dr. Bryce Munger for a study of development of oral mucosal sensory receptors in the rhesus is completed with a comprehensive report, now available through the National Technical Information Service.

BIBLIOGRAPHIC REFERENCES: Biemesderfer, D., Munger, B. L., Binck, J., and Dubner, R.: The Pilo-Ruffini complex: a non-sinus hair and associated slowly-adapting mechanoreceptor in primate facial skin. Brain Res., 142: 197-222, 1978. Munger, B. L. and Ide, C.: The ultrastructural basis for the identification of primate golgi-mazzoni corpuscles (abstract). Anat. Rec. 190: 487, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$40,830

4.0046, A MORPHOLOGIC AND MORPHOMETRIC ANALYSIS OF PRIMATE CRANIOFACIAL GROWTH

O.J. Oyen, Texas A & M University, College Station Campus, School of Liberal Arts, Dept. of Anthropology, *College Station, Texas* 77843 (BNS7825153)

This project involves a comparative structural-functional analysis of the morphology of the upper face in chimpanzees (Pan) and gelada baboons (Theropithecus gelada) based upon procedures and findings derived from a recent study of skull growth in olive baboons (Papio cynocephalus anubis). Results will serve to test the hypothesis that patterns of bone growth during post-natal development of the upper face are directly influenced by growth-related changes and biomechanical lability in the dentomasticatory (tooth-jaw) system.

Specifically, the investigator will: 1. gather data about craniofacial bone surface characteristics and patterns of trabecular organization from cross-sectional collections of chimpanzees and gelada baboons. 2. accumulate correlative craniometric data in order to assess quantitatively growth-related changes in the supra-orbital (brow) region and related masticatory biomechanical parameters. 3. analyze these data to identify any consistent aspects operative in the trabecular organization, osteogenesis, and morphogenesis of the supraorbital region. 4. compare these data with similar information which has already been gathered for olive baboons in order to identify correlative features of upper face development and concomitant growth-related alterations in the masticatory complex, thereby providing evidence of the structural-functional integration of these phenomena in three different primate species.

IV. CRANIOFACIAL ANOMALIES, GENERAL

SUPPORTED BY

U.S. National Science Foundation, Directorate for Biological Behavioral & Social Sciences, Div. of Behavioral & Neural Sciences	$21,951

4.0047, TEETH AND ORAL STRUCTURES

H.E. Evans, Cornell University, Ithaca Campus, New York State College of Veterinary Medicine, Dept. of Anatomy, *825 Veterinary Research Tower, Ithaca, New York* 14853 (NYC-420-329)

OBJECTIVE: Document the chronology and morphogenesis of teeth in the Beagle for the anatomical literature. Obtain data useful in studies of tooth transplantation, organ culture of isolated teeth, eruption phenomena, calcification sequences, and incorporation of radioactive contaminants.

APPROACH: Serial sections and alizarine-stained cleared embryos of known ages will be studied. The material for this study has been collected over several years and includes representative imbryos of almost all stages of gestation.

PROGRESS: Observations on a sizeable collection of purebred canine fetuses of known age has afforded the opportunity to report baseline data on the timing of tooth germ development in the dog. The chronology of development of the deciduous dentition has been studied in a collection of 172 embryos and fetuses from purebred Beagles of known gestation. Serial sections, reconstructions, and alizarin-stained clearings were used. These observations establish that the dental lamina is initiated at 25 days gestation and that calcification begins at 42 days in the deciduous teeth. Horseradish peroxidase (HRP) was injected into salivary glands in 38 neonatal dogs. This enzyme by retrograde axonal transport is conveyed to the cell bodies of neurons terminating in the injected field. After injection of the lingual, mandibular, and sublingual salivary glands, labeled neurons appeared in the dorsolateral part of the medullary reticular formation. These small multipolar neurons were situated dosal to the facial nucleus and ventral to the lateral vestibular nucleus. After parotid salivary gland injections the medullary reticular formation did not label but neurons in the otic.

SUPPORTED BY

New York State Government	funds n.a.

IV. CRANIOFACIAL ANOMALIES, GENERAL

ETIOLOGY - COMPARATIVE SCIENCES

4.0048, DENTAL DESIGN, MASTICATORY EFFICIENCY, AND THE EVOLUTION AND DIETARY SPECIALIZATIONS

R.F. Kay, Duke University, School of Medicine, Dept. of Anatomy, *Box 3711, Durham, North Carolina* 27710 (BNS7708939A01)

The long-term goal of this research is to explain in functional and adaptive terms the morphological diversity and evolution of primate molars. It will clarify the adaptive significance of dental changes which have accompanied the origins of this order and of some of its major subgroups. The present research will deal specifically with two areas: 1. Dental-dietary relationships among living species. This will involve (a), a quantification of the size of chewed food particles and a study of how particle size relates to the design of the molar dentition and (b), morphological and metrical studies of the molar dentitions of living primates to identify features which have been selected in response to specialized feral diets. 2. Studies of the dentitions of extinct primate species with an interpretation of their probable dietary regimes based on part 1. Two special areas of interest are those dental changes accompanying the origins and early radiations of primates and the adaptive significance of the bilophodont molars of Old World monkeys.

SUPPORTED BY

U.S. National Science Foundation, Directorate for Biological Behavioral & Social Sciences, Div. of Behavioral & Neural Sciences	$25,835

4.0049, THE GROWTH AND DEVELOPMENT OF TEETH IN MAN AND OTHER VERTEBRATES

Unknown, Medical Research Council, Dental Unit, *Bristol, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$17,709

4.0050, BUCCAL INNERVATION OF CATS

J.P. Proust, Universite dAix Marseille, Faculte de Chirurgie Dentaire, Dept. of Biology & Fundamental Materials, *Charles Livon Blvd., Jardin Emile Duclaux, 13007 Marseille, France*

The objective of this work is to show the morphological aspect of the buccal terminal nerve structures of the cat in microscopic and electronic optics. This study is carried out in correlation with the electro-physiological research directed by N. Mei and J. Hartmann at the C.N.R.S. concerning these same structures.

Communications already presented on this subject: Innervation desmodontale chez le chat, XXIeme Congres du G.I.R.S.O., Toulouse, April 1977. Capsular cells and oral nerve endings, 14th Annual Meeting of the C.E.D. of I.A.D.R., Rome, September 1977.

SUPPORTED BY

Universite dAix Marseille	funds n.a.

PATHOLOGY - CRANIOFACIAL GROWTH

4.0051, INTERDISCIPLINARY STUDIES - CLEFTS AND OTHER ANOMALIES--NASAL SEPTUM RESECTION AND CRANIOFACIAL GROWTH IN A CHIMPANZEE ANIMAL MODEL

E.J. Forrest, University of Pittsburgh, Cleft Palate Center, *Salk Hall 313, Pittsburgh, Pennsylvania* 15261 (P01 DE 01697-170034)

The objective of the research now being conducted is a longitudinal study designed to investigate the relationship between the growth potential of the nasal septum and the ontogenetic development of the craniofacial complex in chimpanzees. An attempt will be made to quantify the differential effects of age at surgery and amount of nasal septum resected on anterior facial growth retardation. The use of a chimpanzee model will approximate as closely as possible the human condition, where the applicability of such surgery is important for the correction of gross disharmony between the face and jaws as well as in the management and correction of cleft palate.

The procedure will include the use of the Siegel procedure for resection of the nasal septum in chimpanzees. Twelve chimpanzees will be studied during the first year and followed longitudinally thereafter. Three unoperated animals will serve as controls. Evaluation of data will take place during the lifetime of the animals for cephalometric and dental cast data. The influence of nasal septum resection upon facial growth will thus be evaluated.

This project is well under way, and the progress report for the first year is now being compiled. This study is at the point that was anticipated when the program was written.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$36,113

4.0052, ANALYSIS OF PRIMARY PALATE FORMATION

R. Minkoff, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Orthodontics, *Chapel Hill, North Carolina* 27514 (R01 DE 04731-03)

An understanding of primary palate development is necessary for further progress to be made in research related to malformations such as cleft lip and palate. We have chosen the chick embryo as a model system because it permits studies on both cell proliferation and cell migration. Findings from this study will eventually be extended to normal and abnormal primary palate development in mammalian embryos. Embryos will be analyzed from the stages of development beginning with the invagination of the nasal placode, through the stages of formation of the nasal processes up to the time of fusion. Cell proliferation of mesenchyme will be measured by labelling indices, maximum labelling determinations, and by determination of fraction of labelled mitoses through the use of 3H-thymidine incorporation into DNA. These determinations will yield information on the length of the cell cycle, and of its component parts for each of the populations studied, and on the presence of subpopulations differing generation times. The areas to be studied included the lateral and medial nasal processes, the base of the olfactory placode, the maxillary process and the mesenchyme of adjacent areas.

Cell migration into the nasal processes during their development will be studied by the use of transplants between Japanese quail and chick embryos and between 3H labelled donors and unlabelled hosts. The areas to be examined are the same as those listed for cell proliferation studies and pathways of migration as well as rates of migration will be determined.

BIBLIOGRAPHIC REFERENCES: Cell proliferation during morphogenetic change; analysis of frontonasal morphogenesis in the chick embryo employing DNA labeling indices, Robert Minkoff and Amy J. Kuntz, Journal of Embryology and Experimental Morphology, vol. 40, pp. 101-113, 1977.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $78,236

IV. CRANIOFACIAL ANOMALIES, GENERAL

4.0053, CRANIOFACIAL GROWTH AND REMODELING

D.H. Enlow, Case Western Reserve University, School of Dentistry, Dept. of Orthodontics, *2165 Adelbert Rd., Cleveland, Ohio* 44106 (R01 DE 05078-03)

This is a renewal application dealing with determinations of skeletal growth and remodeling patterns in the face and cranium of (a) the normal human and different laboratory species, and (b) the human craniofacial composite having various facial anomalies. The present study is a continuation of projects already in progress and have seven specific objectives. These are, first, to carry out detailed histologic analyses of the craniofacial remodeling patterns in prenatal and postnatal human cadaver material having severe skeletal malocclusions, cleft palate, mandibulofacial dysostosis, Down's, Crouzon's, Apert's, etc. syndromes and to compare and contrast these with normal bony remodeling patterns (as already determined in completed phases of the applicant's studies). Second, to conduct a 'Counterpart Comparison' analysis, using headfilms, of a wide variety of craniofacial anomalies. Third, to study the histological structure of the normal periosteum associated specifically with resorptive growth fields as compared with depository fields. Fourth, to complete a counterpart-comparison study of the Black craniofacial complex. Fifth, to determine the critical timing during which certain major remodeling changes in the incisor region of the human mandible and maxilla take place (known to be some time between birth and the sixth postnatal year), and to evaluate the clinical significance of these events. Sixth, to study the age-related appearance and distribution of secondary osteons in the different bones of the face and cranium. Finally, to carry out a TEM study of collagenous fiber attachment on resorptive periosteal surfaces of growing facial bones and to describe the relinkage process by which these fibers sustain continuous attachment between bone and other fibers located in the enclosing membranes (periosteum, periodontal membrane).

BIBLIOGRAPHIC REFERENCES: Enlow, D.H., and S. Comet-Epstein: A comparative population-distribution study of dental specialists in Ohio. Ohio Dent. J., 53: 3, 34-37, March, 1979. Kurihara, S. and D. Enlow: Remodeling reversals in anterior parts of the maxilla and mandible. J. Dent. Res., 58: 735, 1979., (abstract).

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,

National Inst. of Dental
Research $76,203

4.0054, POSTNATAL DEVELOPMENT OF THE RAT SKULL

J.F. Bosma, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Oral & Pharyngeal Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00181-04 CI)

A PHS Grant Application has been submitted to the National Library of Medicine for subvention of publication of the book, Postnatal Development of the Rat Skull.

In Part 1 of the book, the cranium and mandible of the rat are demonstrated by drawings and photographs at successive postnatal ages. In Part 2, development of the cranium and mandible are demonstrated by alizarin vital staining and photographs of sections. This combination of methods affords comprehensive demonstration of the development of individual bones, of skeletal composites and of the skull as a whole.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $47,032

4.0055, THE MOLECULAR CONTROL OF HUMAN CELLULAR MOVEMENTS - BIOCHEMICAL ASPECTS

R. Niederman, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *1400 Vet. of Foreign Wars Pkwy, West Roxbury, Massachusetts* 02132 (690-001-F)

It has been reported that OsO4 post-fixation for electron microscopy degrades actin filaments (Szamier and Pollard, J. Cell Biol., 1978). We have used native and synthetic rabbit skeletal muscle myosin filaments to test the efficacy of currently recommended protocols which are claimed to preserve actin filaments (Szamier and Pollard, J. Cell Biol., 1978; Begg and Rebhen, J. Cell Biol., 1978; Tilney et al, J. Cell Biol., 1978). Evaluation of fixation was done in three ways: by measurement of filament diameters and lengths from electron micrographs; by changes in fractional relative viscosities; and by SDS gel electrophoresis. Native and synthetic filaments treated with any of the gluaraldehyde protocols appeared to have a similar size (L equals 1.7 u, D equals 16.4 nm), and appearance, as UAc stained filaments. Change in relative viscosity was least with the Tilney fix (% delta equals 0), next with the Begg, Rebhen fix (% delta equals .3) and most with the Szamier Pollard fix (% delta equals 1.4). Gel electrophoresis showed no banding pattern, but had dense precipitates on the surface of the gel. Native filaments treated with OSO4 lost contrast density and aggregated into nets. OSO4 treated synthetic filaments were thinner and darker and displayed heads condensed along the filament backbone. (L equals 1.45 u; D equals 13.5 nm). Change in relative viscosity was least with Szamier and Pollard (% delta equals .1), best with Tilney et al (% delta equals .7) and most with Begg and Rebhen (% delta equals 1.4). Gel electrophoresis revealed breakdown products in the 50-80K dalton range. Filaments treated with glutaraldehyde and OSO4 appeared to be degraded, swollen, and lacked contrast (L equals 1.66 u; D equals 18.5 nm). We conclude that none of the recommended actin fixation protocols are satisfactory for myosin filaments.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

4.0056, CONTRIBUTION TO THE UNDERSTANDING OF THE PALATE LVMPHATIC VESSELS

L.M. Bonaterra, Universidad Nacional de Cordoba, School of Dentistry, Dept. of Anatomy, *University City, 5000 Cordoba, Argentina*

The anatomic distribution of palate lymphatic vessels is being studied, using recently died fetuses from 5 to 9 months and adults as material.

To visualize the lymphatic vessels we inject Dalla Rosa paste (diluted India ink 2:1) and Gerota Blue Mass (Prussian Blue in oil in tubes, Trmentin essence).

The liquid was injected in pre-established points, having observed up till now the existence of a delicate network of lymphatic vessels homo- and heterolateral of anteroposterior direction.

SUPPORTED BY
(No Supporting Organization
Reported) funds n.a.

4.0057, MORPHOGENESIS OF THE TEMPOROMANDIBULAR JOINT

O.J. David, Universidad Nacional de Cordoba, School of Dentistry, Dept. of Anatomy, *University City, 5000 Cordoba, Argentina*

We have tried to visualize the behaviour of the following structures of the temporomandibular joint: mandibular condile, temporal surface, interarticular meniscus, articular capsule and principal ligaments of fetuses from 3 months of intrauterine life to birth. Fetuses fixed in neutral formol pH 7,00 buffer are used as material. The methods used are the dissection and microdissection and the histologic study with coloring of hematoxiline eosine, Masson PAS and Van Gieson.

The inner behavior of the above mentioned structures and the degree of determinism in form to project it in a future piece of work on children and adult remodeling are observed.

SUPPORTED BY

(No Supporting Organization Reported)	funds n.a.

4.0058, A STUDY ON THE OCCURRENCE OF ALKALINE PHOSPHATASE IN THE SUTURA INTERFRONTALIS OF WISTAR RATS

I.S. Markens, Rijksuniversiteit te Utrecht, School of Dentistry, Dept. of Orthodontics, *261-263 Radboudkwartier, Utrecht, Netherlands*

The aim of the present study was to determine the presence of alkaline phosphatase during various stages in development and closure of the sutura interfrontalis. The histological sections reveal that this enzyme could primarily be demonstrated in the dura mater of this suture. In further developmental stages, alkaline phosphatase could be observed with the intermediate zone as well as the pericranium. These findings are brought in relation with the occurrence of synostosis which can be induced under experimental conditions.

SUPPORTED BY

(No Supporting Organization Reported)	funds n.a.

4.0059, THE EFFECT OF IN UTERO, BIRTH AND NEO-NATAL EVENTS ON TOOTH DEVELOPMENT IN MAN

J. Dobbing, University of Manchester, Dept. of Child Health, *Oxford Rd., Manchester M13 9PL, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$11,503

4.0060, CONTROL MECHANISMS IN CRANIOFACIAL SUTURE GROWTH AND REMODELLING - THE BIOLOGICAL BASIS FOR ORTHODONTIC TREATMENT

J.J. Reynolds, Strangeways Research Lab., Dept. of Cell Physiology, *Worts Cswy., Cambridge, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$19,150

IV. CRANIOFACIAL ANOMALIES, GENERAL

4.0061, RADIOLOGIC STUDY IN PATIENTS WITH NEUROENDOCRINE DISTURBANCES

N.R. Acuna, Universidad Nacional de Cordoba, School of Dentistry, Dept. of Radiology, *University City, 5000 Cordoba, Argentina*

This work consists in a radiographical study on dental and bone structures of the head and hand in patients suffering neuroendocrine disturbances.

SUPPORTED BY

Universidad Nacional de Cordoba	funds n.a.

4.0062, A LONGITUDINAL AND CROSS-SECTIONAL STUDY OF ORAL HEALTH - CRANIOFACIAL NORMS IN ADULTS

K.K. Kapur, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *16111 Plummer St., Sepulveda, California* 91343 (665-002-P)

Two full-time technicians have been trained to trace and digitize the cephalometric radiographs. The lateral head films in the mandibular occlusal and rest positions and the frontal head films for the first and second cycle examinations of over 250 of the 294 subjects with complete dentition (control group) have already been traced. Approximately 400 tracings have been digitized and checked for accuracy. We plan to complete the tracing and digitizing of 380 remaining films by the end of July, 1979. We also expect to enroll the additional 44 subjects into the control group and have their first cycle films traced and digitized by the end of September, 1979. The methodology for making measurements of the maxillary and mandibular casts has been developed and the necessary photographic equipment has been ordered.

A preliminary study was undertaken to determine changes, associated with aging and with loss of teeth, in the inferior cortical mandibular border and the inferior aspect of the mandibular symphysis. The mean thickness and area of the inferior cortical border increased with age, both in dentulous and adentulous subjects, but the cortical layer was markedly thinner in denture wearers than in sbjects with natural dentition. On the other hand, cortical thickness in the inferior aspect of the mandibular symphysis decreased in thickness with age especially in the natural dentition group and was thicker in denture wearers than in subjects with natural dentition. The apparent disparity at the two sites indicates that bone remodeling at the inferior mandibular border may be caused by the differences in functional bone stresses induced by the two types of dentition rather than being attributed solely to generalized aging.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

PATHOLOGY - PHYSIOLOGY

4.0063, FLUX OF IONS INTO DEVELOPING ENAMEL

J.W. Bawden, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Pedodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130151)

The objective of this work is two-fold. The first objective is to further define the mechanisms which control the mineralization of enamel. Cellular control of calcium influx is of particular interest, along with means by which the organic matrix is removed as maturation proceeds.

The second objective is to study the uptake of certain trace elements in various stages of enamel formation. Emphasis is placed on those trace elements which may influence enamel resistance to dental caries.

Experimental methods involve both in vivo and in vitro techniques.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $64,458

4.0064, TRACER AND FINE STRUCTURE STUDIES OF THE ENAMEL ORGAN

E.A. Kallenbach, State University System of Florida, University of Florida, School of Medicine, Dept. of Anatomy, *1600 Archer Rd., Box J-266, Gainesville, Florida* 32610 (R01 DE 02241-14)

The distribution of the large molecular weight tracer horseradish peroxidase is studied after intravenous injection in the enamel organ of the rat incisor with the electron microscope. The different zones of the enamel organ (differentiation, secretion, transition, maturation) are studied separately, and the functional implications of the results are considered for each zone.

The cytology of tetracycline-induced abnormalities in the rat incisor enamel organ is studied with light and electron microscopes. The induced structural and functional abnormalities make it possible to improve present hypothesis of enamel formation and properties of enamel.

The development of the ameloblast-odontoblast relationship is studied in the differentiation zones of the teeth of nurse shark and 3 species of anurans. The presence or absence of basal lamina at the time of enamel deposition is noted, and tracer studies are performed to find whether secretory material (of ameloblasts or odontoblasts origin) crosses the intact basal lamina.

BIBLIOGRAPHIC REFERENCES: Kallenbach, E. Fine structure of stratum intermedium, stellate reticulum and outer enamel epithelium in the enamel organ of the kitten. J. Anat. 126:247-260, 1978.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $21,575

4.0065, STUDIES ON PROTEINS INVOLVED IN DENTINOGENESIS

W.T. Butler, University of Alabama in Birmingham, School of Dentistry, Dept. of Biochemistry, *1919 7th Ave. S., Birmingham, Alabama* 35233 (R01 DE 05092-01)

The transformation of predentin to dentin takes place at a distinct site away from the periphery of odontoblasts and must be a finely controlled process. Biochemical, autoradiographic and morphologic data suggest that certain proteins made by odontoblasts are involved in this process.

In order to gain further insight into the mechanisms of their involvement in dentinogenesis and mineralization, the biosynthesis and deposition of collagen, phosphoprotein and glycoproteins will be studied. These biochemical and autoradiographic studies will be performed with an odontoblast culture system developed in this laboratory. Simultaneously, further investigations on the biochemistry of collagen, phosphoprotein and glycoproteins found in dentin will be conducted.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $86,545

4.0066, MOLECULAR CHARACTERIZATION OF ODONTOGENESIS BY BRDU

S.A. Schwartz, University of Chicago, School of Medicine, Dept. of Pathology, *5801 S. Ellis Ave., Chicago, Illinois* 60637 (R23 DE 04970-02)

This application is submitted to fulfill requirements of the Special Dental Research Application program as described in NIH Guide Vol. 5 No. 20, Date 11-30-76.

We plan to identify and characterize the genetic program for normal and pathological odontogenesis in the rat embryo dental organ. The molecular contributions of interacting dental epithelium and mesenchyme will be individually determined following developmental arrest in vitro resultant from 5-bromodeoxyuridine (BrdU) treatment. Odontogenesis and organogenetic differentiation will be analyzed by morphologic, histologic, and biochemical criteria as measured in rat dental primordia grown in the absence and presence of a nontoxic, bioactive dose of BrdU. We plan as well to localize the distribution of bromouracil within epithelial and mesenchymal DNA nucleotide sequence elements. This information will be compared to the concurrent and simultaneous induction of a latent, endogenous type C RNA tumor virus elicited by the BrdU exposure. It is planned to specifically identify the germ layer source of the virus, as well as any potential molecular correlation between BrdU-mediated developmental arrest and simultaneous virogenic activation.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $27,375

4.0067, ROLE OF NERVES IN DENTINOGENESIS

J.K. Avery, University of Michigan, Ann Arbor Campus, School of Dentistry, Dept. of Oral Biology, *Ann Arbor, Michigan* 48104 (R01 DE 01604-16)

Current studies are directed toward a definition of the total nerve supply to the teeth and to gain information on the possible role of the nerves in teeth to dentinogenesis. The initial objective is being carried out by the study of the trigeminal, otic, pterygopalatine, submandibular, cervical sympathetic ganglia and the mesencephalic nucleus of the trigeminal nerve in the pons after injection of H3-HRP (horseradish peroxidase) in tooth pulps. The mesencephalic nucleus is also being studied using quantitative autoradiography and anterograde transport of H3-leucine, by testing for the presence and distribution of the radiolabeled amino acid in the tooth pulp. Studies are also in progress in which the sensory component of the mandibular nerve is sectioned unilateraly. Tooth pulps are then stimulated bilaterally (by cavity preparation) and changes in the proliferation of the cellular components (pulpal fibroblasts and odontoblasts), using H3-thymidine, are determined relative to the repair of the wound (cavity prep).

IV. CRANIOFACIAL ANOMALIES, GENERAL

BIBLIOGRAPHIC REFERENCES: Chiego, Jr., D.J., C.F. Cox, and J.K. Avery. 1978. An autographic analysis of H3HRP retrograde transport and localization within neuronal cell bodies innervating primate dental pulps. Am. Assoc. of Anat. 190, pg. 163. Cox, C.F. and J.K. Avery. 1978. Graphic distribution of adrenergic nerve endings in mouse molar pulps. J. Dent. Res. 57, Spec. Issue A, p. 207, Abst. 532.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $61,326

4.0068, COMPARISON OF PSYCHOPHYSICAL MEASURES OF HUMAN SOMESTHETIC CAPABILITIES OBTAINED FROM VOLUNTEERS WITH NORMAL & ABNORMAL NEUROLOGICAL FUNCTION

D.A. Dreyer, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Oral Surgery, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130204)

The objective of this project is to obtain quantitative measures of somesthetic capabilities of neurologically intact and abnormal humans using controlled tactile stimuli. Stimuli are delivered via a computer-controlled servo-motor system capable of moving a brush across the skin at velocities ranging between 0.5 and 300 cm/sec in either of two directions. Tactile discrimination ability is measured by determining subjects' ability to correctly identify direction of brush motion as a function of brush velocity and length of skin contacted by the brush (traverse length). Data are reported in terms of 'critical traverse length', i.e., that length of skin which must be contacted by the brush at a given velocity in order for the subject to respond correctly in at least 75% of the trials. We have characterized discrimination ability in normal individuals for the hand, arm and orofacial region and found performance to be optimal at velocities between 3 and 25 cm/sec. We are presently in the process of collecting similar data from patients with defined neurological deficits such as produced by neurolysis procedures for relief of pain or iatrogenic complications from procedures such as saggital split osteotomy.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $69,634

IV. CRANIOFACIAL ANOMALIES, GENERAL

4.0069, A MOLECULAR GENETIC APPROACH TO OLFACTION

S. Price, Virginia Commonwealth University, School of Basic Sciences & Graduate Studies, Dept. of Physiology, *901 W. Franklin St., Richmond, Virginia* 23284 (R01 DE 04271-04)

In this project we hope to isolate one or more odor receptor molecules, and to map their distribution in mice at the levels of gross anatomy, histology, and ultrastructure. The approach is based on using strains with hereditary specific anosmias to prepare antibodies against the receptor sites. The antibodies will then be modified for use as strains and as affinity chromatography materials. Thus, we hope to make a major contribution to the understanding of this aspect of craniofacial functions.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $66,235

4.0070, ORAL REFLEXES OF THE INFANT

J.M. Weiffenbach, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Oral & Pharyngeal Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00124-06 CI)

The discrete elicited lateral tongue movement of the human newborn first described under this project continues to be used in psychophysical studies of oral sensation. The transverse tongue reflex described previously can be elicited by separate 5 microliter drops of fluid. The reflex adapts to repeated fluid elicitations. In earlier studies, the response returned when glucose in suprathreshold concentration was added to the stimulus fluid after adaptation to water. This experimental sequence thus indicates taste discrimination. Current studies address the question of sensitivity to the salty taste and its relation to sensitivity to sweet.

BIBLIOGRAPHIC REFERENCES: Weiffenbach, J. M.: The Development of Sweet Preference: Proceeding, Sweeteners and Dental Caries, Eds. Shaw, J. H. and Roussos, G. G., Sp. Supp. Feeding, Weight and Obesity Abstracts, 1978, pp. 75-91.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $22,332

4.0071, STUDIES OF SENSORIMOTOR IMPAIRMENTS OF THE MOUTH AND PHARYNX

J.F. Bosma, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Oral & Pharyngeal Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00182-04 CI)

Persons who have disorders and/or impairments of feeding, speech, or airway patency are evaluated by standard and cinema photography, and standard and cinema radiography.

Currently, principal attention is directed toward persons who have neurologic impairments of the mouth and/or pharynx. Persons having impairments in this area in association with malformation, cancer or cancer surgery, or inflammatory disease are also under study.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $41,296

4.0072, TASTE AND ITS DISORDERS

R.O. Wolf, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Oral & Pharyngeal Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00212-03 CI)

The selection and refinement of appropriate psychophysical methods for the separate measurement of the various aspects of taste perception is a primary and continuing concern of this project. Normal variation in taste perception with chronological age is being assessed by procedures which quantify the intensity and pleasantness of the subject's taste experience. Parallel studies are concerned with anomalous taste experience as a naturally occurring phenomenon or as a consequence of experimental manipulation of diet. Other studies are directed specifically at taste perception difference between individuals with and without caries.

BIBLIOGRAPHIC REFERENCES: Jam, I., Shoham, M., Wolf, R.O. and Mishkin, S.: Elevated serum amylase activity in the absence of clinical pancreatic or salivary gland disease. Amer. J. Gastroenterol. 70:480-488, 1978. Wolf, R.O. and Taussig, L.M.: Letter to the editor: Serum Salivary Amylase in Cystic Fibrosis. Pediat. Res. 13: 1076, 1979.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $69,203

4.0073, DEVELOPMENT OF THE SENSE OF TASTE

R.M. Bradley, University of Michigan, Ann Arbor Campus, School of Dentistry, Dept. of Oral Biology, *Ann Arbor, Michigan* 48104 (BNS77-09920 A02)

The development of the sense of taste in sheep will be studied to determine when this sensory system becomes functional and to describe any changes in taste function during development. Neurophysiological recordings of taste responses will be made in the medulla of fetal, newborn and adult sheep while the tongue is stimulated with chemicals. These neurophysiological data will be correlated with information on the structure of developing taste buds.

The role which early, intrauterine, taste experience may play in influencing the formation of adult taste preferences will also be studied. Fetal lambs will be exposed for a major part of gestation to chemical infused into the amniotic fluid. At birth the lambs will be tested to determine the effect of the infused chemical on taste preference-aversion behavior.

SUPPORTED BY
U.S. National Science
Foundation, Directorate for
Biological Behavioral & Social
Sciences, Div. of Behavioral &
Neural Sciences $49,600

DIAGNOSIS & TREATMENT - CRANIOFACIAL MEASUREMENT

4.0074, DIGITIZATION OF ROENTGEN-CEPHALOMETRIC DATA

S. Pruzansky, University of Illinois, Medical Center at Chicago, Abraham Lincoln School of Medicine, Dept. of Pediatrics, *1853 W. Polk St., Box 6998, Chicago, Illinois* 60680 (P01 DE 02872-100034)

The CCFA plans to develop a general system through which selected roentgencephalograms may be digitized and stored so that the data will be readily available for comparisons and research projects. This system must be flexible enough so that new researchers with new projects will be able to adapt it to their own needs. At this time the hardware required for digitizing has been acquired. The software, consisting of basic functions and subroutines which allow us to write programs for our own particular tasks, has been received from UCLA. These programs are now in operation. Next we must write programs to do the specific tasks we require.

We accumulated significant numbers of tracings of cephalograms which have been digitized. At present we are working on a special project of CPI (Congenital Palatopharyngeal Incompetence) patients. This is a prototype project for validation of methods. We are expanding into other categories of patients using a task-oriented approach at first.

Added normative data. Protocol applied to analysis of pharyngeal area in patients with Apert and Crouzon syndromes. Study of longitudinal growth of tonsils and adenoids in various cleft types underway.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $30,019

4.0075, CRANIOFACIAL ANOMALIES - ETIOLOGY AND TREATMENT (CRANIOFACIAL MEASUREMENT)

J.M. Converse, New York University, School of Medicine, Dept. of Surgery, *550 1st Ave., New York, New York* 10016 (P01 DE 03568-050009)

OBJECTIVES: Linear and angular measurements of skeletal cranial and facial structures obtained from lateral and postero-anterior cephalograms will be used to document characteristics (constants and variables) of each anomaly.

APPROACH: Cranial base measurements include distances and angles involving sella-basion- and nasion. They will be used to determine the degree and direction of cranial base growth. A correlation between the character of cranial base growth and the accompanying facial development will be documented. Angular measurement of the upper face will be correlated with the degree of angular flexion of the cranial base (i.e., basion-sella-nasion). Lower face measurements involving mandible as an entity are as follows: (Articulare-Gonion, Gonion-Gnathion, Articulare-Gnathion and posterior symphyseal shadow to Pogonion). Other measurements to be taken are: Nasopharyngeal (linear measurements) for height, depth and width. Interorbital distance measurements (taken between the external lacrimal crests) from the postero-anterior cephalograms for patients with orbital hypertelorism. Other areas follow: a) bi-sphenoid distance, b) height of the orbit, and c) width of the orbit taken at three different levels.

CURRENT PLANS: 1. To determine what, if any, common anatomical characteristics may be specific for each craniofacial anomaly under study. 2. Document rate and patterns of craniofacial growth within each anomaly. 3. Use the data to serve as a guide in establishing the optimum time for surgical intervention.

PROGRESS: Linear and angular measurements have proved to be useful in defining the degree and character of the various anomalous structures under study. Preliminary reports indicate that the data is significant in assessing the impact of surgery and/or growth on the craniofacial complex.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$58,540

4.0076, INTEGRATED THREE-DIMENSIONAL CRANIOFACIAL MEASUREMENT

S. Baumrind, University of California, San Francisco Campus, School of Dentistry, Dept. of Orthodontics, *551 Parnassus Ave., San Francisco, California* 94122 (R01 DE 03703-04)

The aim of this project has been to develop and refine a new photogrammetric method for constructing three-dimensional craniofacial maps by means of the computer conducted merging of coordinate data from stereopairs of lateral and frontal skull x-ray films ('cephalograms') with coordinate data from stereophotographs of dental study casts and of the face. Quantitatively precise integration of the data from these different types of record is obtained by placing triads for radiopaque metal 'tie-in points' in the mouth and on the surface of the face in such manner that they can be seen on both the cephalograms and the photographs.

During the past period we have designed and constructed the basic hardware and software necessary to test the utility of this method. Preliminary tests indicate that it is feasible and practical and is probably more powerful than any conventional method now in use, but the operational limits of the method and of our physical system have not yet been fully tested. During the present phase of the project we intend to refine our existing photographic and radiographic hardware, to expand and refine our computer software, and to conduct empirical tests of the accuracy and reliability of both the radiographic and photographic components of the system under clinical conditions.

This project was originally undertaken in order to develop a system for the longitudinal study of anatomic changes following surgical corrections of craniofacial anomalies and gross malocclusions, and for studying the effects of conventional orthodontic treatment. It now appears likely that this approach will have other uses in medicine, anthropology, and elsewhere as a relatively non-destructive general means of homogeneous non-radiopaquebody.

During the past eighteen months the method has been used as a means of detecting looseness in total hip prostheses.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$69,373

4.0077, AUTOMATED PHYSIOPRINTING OF FACIAL PATTERN

V. Sassouni, University of Pittsburgh, School of Dental Medicine, Dept. of Orthodontics, *C336 Salk Hall, Pittsburgh, Pennsylvania* 15213 (R01 DE 04584-02)

At this time, there is no practical, accurate, rapid and economical quantitative method of measuring the soft tissue appearance of the face. At the same time, many treatment decisions in orthodontics, maxillo-facial surgery, dento-facial prosthesis, are based on a subjective evaluation of facial balance.

The objectives of this proposal is to combine the physioprint, a standardized photographic technique, with automatic optical scanner to record and compute the facial pattern in three dimensions.

The five-year project is subdivided in the following manner: 1st year: Improvement of the physioprinting and its processing with automated optical scanner for quantitative data collection in three dimensions - Estimate of errors - Reduction of coordinates to the most meaningful ones (Parsimony). 2nd and 3rd Years - Application of the system for the establishment of facial soft tissue 'standards of normality' (in terms of association with normal occlusion) and of facial esthetic standards - These will have a major value for diagnostic and reference purposes. 4th year - Application of the system for the epidemiology of extreme facial variations in order to assess the nature and the severity of the soft tissue deviations. This study may provide criteria to determine 'handicapping malocclusion'. It also may give criteria for distinguishing patients in need of maxillofacial surgery rather than orthodontics. 5th Year - Initiate the application of this technique for the study of treatment effect on the face. This initial start into treatment may be followed by a second five-year project for the application of the technique to the diverse orthodontic, surgical or prosthetic treatment of dento-facial abnormalities.

The advantages of this system are its capabilities in recording, measuring and storing automatically large numbers of three-dimensional facial soft tissue measurements. Because the external soft tissue is closely the expression of underlying bone and teeth, this system may become, in part, a substitute for roentgenographic cephalometry, thus reducing radiation hazard to the population, without reduction of diagnostic information.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

4.0078, CEPHALOMETRIC DESCRIPTION OF GROWTH PROCESSES THROUGH THE USE OF SYMMETRIC AXIS CODING

R.L. Webber, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Diagnostic Methodology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00158-05 CI)

A geometric method for isomorphically transforming the shape of biological structures expressed as two dimensional projections is being applied to tracings of cephalograms to determine constraints underlying growth and development. The rationale underlying this effort is based on the assumption that the relatively small amount of systematic progress in quantitative morphology may be attributed to a lac of coordinate independent bases for mathematical description.

Symmetric-axis geometry provides a promising alternative to conventional cephalometric descriptions which has lead to the discovery of fixed angular relationships in lateral projections of the human mandible. The associated angles appear to be independent of age within and between individuals. Preliminary findings applied to the mandibular shape of other species suggest that homologous angles may be invariant likewise.

BIBLIOGRAPHIC REFERENCES: Blum, H. and Nagel, R. N.: A symmetric Axis Basis for Object Recognition and Description. Pattern Recognition (1979).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$75,646

IV. CRANIOFACIAL ANOMALIES, GENERAL

DIAGNOSIS & TREATMENT - CRANIOFACIAL GROWTH

4.0079, CRANIOFACIAL ANOMALIES - ETIOLOGY AND TREATMENT OF CRANIOFACIAL GROWTH (GENERAL)

J.M. Converse, New York University, School of Medicine, Dept. of Surgery, *550 1st Ave., New York, New York* 10016 (P01 DE 03568-050006)

This program is designed to evaluate and to document the specific anatomic deformities and functional disabilities which characterize each of the various syndromes in craniofacial anomalies and, through carefully controlled longitudinal growth studies in patients admitted to the project at different age levels, to determine the optimal timing and temporal sequence of reconstructive surgical procedures in craniofacial anomalies. It includes surgical-orthodontic-prosthodontic reconstructive therapy at different age levels in each of the major categories of craniofacial anomalies and detailed studies of the effect of early surgery on craniofacial growth and morphology. Special attention is being focused on the early surgical manipulation of craniofacial sutures in patients with craniofacial dysostosis.

Included in these studies are study of extraocular muscle and retinal function in patients with craniofacial malformations, evaluation of neurological deformities in these patients, radiographic and pathological evaluation of temporal bone status, psychosocial and psychometric evaluation including the impact on this function by rehabilitation, audiometric studies of middle ear and inner ear anomalies associated with congenital facial malformations, assessment of speech before and after surgery and genetic studies including complete family history, pedigree analysis and examination of patients to detect consistent differences in the phenotype of patients with similar syndromes.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$343,128

4.0080, CRANIOFACIAL ANOMALIES - ETIOLOGY AND TREATMENT OF CRANIOFACIAL GROWTH

J.M. Converse, New York University, School of Medicine, Dept. of Surgery, *550 1st Ave., New York, New York* 10016 (P01 DE 03568-050008)

OBJECTIVES: To determine the patterns of craniofacial growth in children with craniofacial anomalies. The rate and patterns of growth for the cranium, maxilla and mandible in affected subjects will be analyzed on a time basis. This data will be compared to normative data compatible for age and sex. The impact of growth on one or all of these areas will be evaluated and correlated with the clinical examination of the patient.

APPROACH: Analysis of cephalometric tracings in the form of linear and angular measurements will be done on a longitudinal basis to assess the characteristics of the anomaly within the skeletal and soft tissue structures of the cranium and face. These measurements, taken once a year, will serve to help us in charting the rate and patterns of craniofacial growth. The assessment of the interrelationships of facial structures will assist us in defining degrees of facial imbalance.

CURRENT PLANS: Growth data will be studied and compared to normative data used in determining the optimum time for corrective surgery of craniofacial anomalies.

PROGRESS: Our preliminary data reflects that in subjects with craniofacial anomalies with some degree of variability the following appear to be consistent and common findings: 1. Abnormal dimensions in anterior and posterior cranial base. 2. Hypoplasia of the maxilla in its vertical and horizontal dimensions. 3. The abnormal location of these structures (cranial base and maxilla), on a time basis, from infancy to adulthood. 4. The abnormal nasopharyngeal dimensions (height and depth) consistent with the failure of maxilla to locate inferiorly and vertically. 5. Discernible mandibular growth potentials in patients with abnormalities of the mandible have been noted.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$60,279

4.0081, SURGICAL EFFECTS ON CRANIOFACIAL GROWTH AND DEVELOPMENT

T.H. Hohl, University of Washington, School of Dentistry, Dept. of Oral & Maxillofacial Surgery, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (R01 DE 04478-03)

The long-term objectives are to undertake studies of craniofacial growth and development following surgical intervention. Alterations in facial growth and development in human subjects will be evaluated following surgical intervention using a photocephalometric technique, as well as by metallic implants and laminographic radiographs. In addition, primate studies will be utilized to determine the effects of early mid-facial surgery and masticatory muscle transpositions on the growth of the craniofacial complex.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

4.0082, A STUDY OF GROWTH OF NORMAL AND ABNORMAL FACES

R.E. Shaw, University of Connecticut, Storrs Campus, School of Liberal Arts & Sciences, Dept. of Psychology, *Storrs, Connecticut* 06268 (R01 DE 04990-01)

The major long range goal of Project Fate is research and development aimed at discovering the physical and biological determinants of the information underlying the perception of the growing and aging human face. Once discovered, the perceptual information will be mathematized and formally incorporated into a computer graphics system (the FATE Program) aimed at simulating the interaction of cosmetological treatments with the growth and aging of cranio-facial complex. Because of the complexity of this problem, Project FATE participants are drawn from a wide range of disciplines: psychology, orthodontics, oral and maxillary surgery, mechanical engineering, mathematics, art and computer science. The development of the FATE Program will require efforts at three levels of research: theoretical, empirical and clinical. As the subprograms for simulating growth, aging and treatment effects are developed, each will be subjected to thorough empirical validation procedures to ensure the scientific accuracy and clinical usefulness of the displays. To achieve these ends Project FATE comprises three task-forces of experts who will assume responsibility a) for the development of the simulation program and its empirical validation, b) for the research to discover the physical and biological determinants of the perceptual information for aging and growth of the face, and c) for the research to determine the most natural representation of the human face to be graphically displayed for scientific and clinical purposes.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$107,097

4.0083, PATTERNS OF DENTOCRANIOFACIAL GROWTH AND MATURATION

A.F. Roche, Wright State University, School of Medicine, Dept. of Pediatrics, *Colonel Glenn Hwy., Dayton, Ohio* 45431 (R01 DE 05160-03)

Dentocraniofacial variables, with emphasis on the cranial base, cranial vault, maxilla and mandible will be studied in normal children. Long-term growth patterns of individual children will be analyzed using well-established and more recent statistical techniques. The study will include interrelationships between variables at particular ages, changes in these relationships across age and the effects on growth patterns of factors that influence other aspects of physical growth. The existing long-term serial cephalometric radiographs allow analyses of secular changes and intrafamilial studies relevant to genetic effects (e.g., parent-child comparisons); the latter will be studied also employing recorded genetic markers. The effectiveness of serial data, of recorded maturity ratings, e.g., skeletal age, menarche, and of mathematical models in craniofacial growth in children with hypopituitarism. The findings will be valuable to human biologists and will assist the clinical work of orthodontists, pediatricians, nutritionists and speech therapists. These professional groups require additional knowledge of craniofacial growth, its correlates, determinants and accurate prediction.

BIBLIOGRAPHIC REFERENCES: Roche, A.F., Roberts, J. and P.V.V. Hamill. Skeletal maturity of youths by racial and socio-economic factors, 12-17 years. Vital Health Statistics, National Center for Health Statistics, Series 11, No. 167, 98 pp. 1978. Roche, A.F. Growth assessment in abnormal children. Kidney International, 14:369-377, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$130,105

4.0084, EFFECTS OF VOMER SURGERY ON MIDFACIAL GROWTH

T. Wada, University of Iowa, School of Dentistry, *Jessup Hall, Iowa City, Iowa* 52240 (R23 DE 04922-01)

Past reports have suggested that surgical trauma to the vomer during some types of cleft palate surgery may be responsible for inhibition of anteroposterior growth in the middle face. The question has been neglected; it has important clinical implications, and additional evidence is needed. In an effort to gain information about the possible influences of vomer surgery on facial growth, 24 weanling beagle dogs will be used in a 9-month longitudinal study of the effects of vomer resection. One group of 8 pups will have surgery, at the end of the 6th postnatal week, for resection of the major part of the vomer. The surgical approach will be via an access flap in the hard palate. Eight other pups will have surgery simulating that for resection, but the vomer will be left in place. A third group of 8 pups will serve as unoperated controls. Sampling will provide that each group will contain 8 unrelated pups, but that each pup will have a like-sex littermate in each of the other two groups. All pups will have tattoo marker points in the mucosa of their hard palates to enable monitoring for contraction during healing of the access flaps. Facial growth will be monitored throughout the study by x-ray cephalometry, maxillary and mandibular casts, and photography. Four additional pups will have vomer resections with subsequent sacrifice, with littermate controls, at intervals of 2, 4, 8, and 12 weeks after surgery. Tissues will be examined by light and electron microscopy in an attempt to gain information about causal mechanisms of the expected midfacial growth inhibition. The suggestion that newly identified contractile cells known as myofibroblasts might be involved in initiation of the anticipated morphogenetic aberration will be examined.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

DIAGNOSIS & TREATMENT - GROWTH PROMOTING FACTORS

4.0085, STUDIES OF ANDROGEN METABOLISM AND ACTION IN RODENT SUBMAXILLARY GLAND

J.C. Coffey, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Endodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130090)

The objective of this proposal is to define the mechanisms of androgen hormone regulation which are important in the development and maintenance of submaxillary gland (SMG) function.

The steroid metabolizing capability of the SMG will be assessed by: (a) Defining the pathways of androgen metabolism in rat, mouse, and monkey SMG in vitro and rat SMG in vivo; (b) Describing maturational changes in SMG androgen metabolism; (c) Studying the effects of hypophysectomy, castration, and hormone replacement on androgen uptake and metabolism in rat SMG. Following either incubation of various labeled androgens with SMG or injection of labeled androgen into animals, the SMG will be extracted and steroid metabolites quantitated by scintillation counting following thin-layer chromatography. Further identification and quantitation of steroid metabolites will be achieved by further thin-layer chromatography, derivative formation, and crystallization.

The site(s) of androgen uptake and metabolism within the SMG and metabolism within the SMG of rats and mice will be determined using dry-mount autoradiographic techniques.

Intracellular androgen receptors in SMG will be identified and their physiochemical properties determined by ultracentrifugation, polyacrylamide gel electrophoresis, and gel filtration on Sephadex G-200. Animals of varying age will be used to determine when the receptor proteins first appear and if they are androgen dependent.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $71,522

DIAGNOSIS & TREATMENT - PHYSIOLOGY

4.0086, INTERDISCIPLINARY STUDIES - CLEFTS AND OTHER ANOMALIES - AN INVESTIGATION OF NORMAL LATERAL PHARYNGEAL WALL MOTION

E.J. Forrest, University of Pittsburgh, Cleft Palate Center, *Salk Hall 313*, *Pittsburgh*, *Pennsylvania* 15261 (P01 DE 01697-170031)

The purpose of this study is two-part: (1) to investigate the mechanism of normal lateral pharyngeal wall motion for velopharyngeal closure and (2) to validate the radiographic image of velopharyngeal structures. The studies will be carried out during both speech and swallowing, and data from videofluoroscopic and videoendoscopic findings will be compared.

Five groups with six subjects each will be utilized. The groups will be made up of adults with unrepaired clefts of the soft palate, with total or partial surgical or traumatic ablation of the soft palate, with surgical alteration of the lateral pharyngeal wall in the naso- and oro-pharynx in the area of velopharyngeal closure, with radical maxillectomy, and with exenteration of one of the orbits so that visualization of velopharyngeal structures is possible.

This study is proceeding as planned in the original project application. No data are available for publication at this time.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $9,559

4.0087, ELECTRON MICROSCOPIC EXAMINATION OF THE EPIDERMIS AND CUTANEOUS APPENDAGES IN CUTANEOUS DYSMORPHOGENESIS

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Previous studies from our Center reported the gross and microscopic aspects in the cutaneous changes in the EEC, OFD and TRP syndromes. It has become apparent that hypertrophic lesions which may look quite dissimilar may have a common origin or pathogenesis and we have reclassified the epidermal nevi accordingly. It now becomes appropriate to identify more refined discriminating features of these entities, and we are undertaking the study of the epidermis and appendages of the same disease groupings by electron microscopy.

Biopsy specimens are first fixed in 20% glutaraldehyde and post-fixed in 1% osmium tetraoxide. The tissue is then rinsed in buffer, dehydrated in increasing concentrations of ethanol, washed with propylene oxide and embedded in a hard mixture of epoxy resin. The embedded tissue is trimmed by hand to 5 mm size. (1) Thick sections (approximately 2.6 x 10 to the 3rd power A) are cut and stained with toluidine blue to determine desired orientation of the tissue. (2) Silver sections or sections between 6 and 9 x 10 to the 2nd power A thickness are then cut, stained with uranyl acetate and post-stained with lead citrate. Stained sections are viewed under a Hitachi 11B electron microscope. Observed areas which are of interest to the investigator are photographed and printed as a permanent record.

This study has been completed, in part, and submitted for publication about three weeks ago. Reduction in budget will be sufficient to terminate this project.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,

best copy available

National Inst. of Dental
Research $9,404

4.0088, GROWING CAPILLARIES - BASAL LAMINA AND PERMEABILITY

R.V. McKinney, Medical College of Georgia, School of Dentistry, Dept. of Oral Pathology, *1459 Gwinnett St., Augusta, Georgia* 30902 (R01 DE 03486-06)

This proposed research is designed to gain further knowledge about the mechanisms of wound healing, the role of the microcirculation in the healing process, and the modulating effects of inflammatory mediators on the microcirculation. Particular attention will be directed toward: (1) The measurement of the permeability characteristics of regenerating wound capillaries; (2) quantitation of the effects of various inflammatory mediators on microvasculature permeability; (3) the development of an in vivo model system for measurement of the above two objectives; (4) the determination of the type of molecular size permeability of regenerating and normal skeletal muscle capillaries; (5) fine structural characterization and functional interpretation of the regenerating capillary endothelium and its basal lamina; (6) the role of vitamin C deficiency on the structure, growth, and permeability of regenerating and normal capillaries; (7) quantitation by microchemistry of the glycosaminoglycans groups in normal, wounded, and vitamin C-deficient guinea pig skin; (8) determination of carbohydrate histochemical data from healing skin wounds; and (9) observations on the fine structure and histochemistry of the mechanisms of epithelial keratinization in healing wounds.

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Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

4.0089, STUDIES IN ORAL PHARYNGEAL REFLEXES

L.J. Goldberg, University of California, Los Angeles Campus, School of Dentistry, Dept. of Anatomy, *405 Hilgard Ave., Los Angeles, California* 90024 (R01 DE 04166-11)

The objective of this research program is to increase our understanding of how the central nervous system controls and coordinates activity in the jaw muscles for the production of complex motor behaviors such as chewing. In humans, single motor unit electromyography will be used to study the function of the muscles of mastication. At various times during the production of precisely controlled voluntary tasks stimuli will be delivered to trigeminal sensory receptors to determine the effects of this peripheral input on the centrally programmed movements. Analysis of recruitment patterns, contractile properties and spike train characteristics of single motor units will be used to determine the mechanisms by which the nervous system codes for the sequence and intensity of contraction of the various muscles of mastication. These techniques will be used as well to determine the role of the nervous system in the establishment of the 'rest' position of the mandible. Patients with the myofascial pain-dysfunction syndrome will also be studied. The characteristics of muscle function established in normal subjects will be compared with those of patients with this syndrome in order to establish the nature of the neuromuscular disorder which leads to the motor disability.

Neurophysiological studies will focus on the use of the guinea pig as an experimental model for study of the interaction of the central nervous system pattern generators responsible for producing rhythmic masticatory movements with the reflex effects of peripheral feedback which results from those movements. Intracellular recording in motoneurons which control the muscles of mastication will be obtained during rhythmic masticatory movements and chewing behavior and will permit analysis of inhibitory and subthreshold excitatory events not observable with any other method. This technique is extremely useful in the study of motor control since the membrane characteristics of motoneurons innervating a particular muscle can be observed during the actual performance of behaviors in which that muscle is involved.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $120,963

4.0090, ADAPTATIONS TO CHANGES IN MASTICATORY MUSCLE LENGTH

J.A. McNamara, University of Michigan, Ann Arbor Campus, Center for Human Growth & Development, *Ann Arbor, Michigan* 48104 (R01 DE 04227-05)

This study is designed to further investigations of adaptive changes in skeletal muscle tissue associated with alterations in muscle length. Alterations in muscle length occur normally during growth, but also can be induced by modifications of the intermaxillary space and by orthognathic surgical procedures. Our primary objective is to broaden our understanding of the structure and function of the muscles of the craniofacial musculature resulting from alterations in resting length, and/or from muscle detachment.

Specific structural and functional adaptations will be produced and investigated by histochemical, biochemical, anatomical and physiological techniques, which we have used previously in studies of craniofacial adaptation. Data and interpretations gained from this study will be combined with data gained from our previous experimental investigations, leading to a better understanding of musculoskeletal adaptations in the craniofacial region.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$87,668

4.0091, MUSCULAR DISORDERS IN CRANIOFACIAL MALFORMATIONS

A.J. Miller, University of California, San Francisco Campus, School of Dentistry, Dept. of Growth & Development, *551 Parnassus Ave., San Francisco, California* 94122 (R01 DE 04940-02)

The objective is to delineate the relationship between deviant skeletal morphology and neuromuscular dysfunction in subjects with craniofacial anomalies.

Patients with craniofacial anomalies who are being treated or evaluated in the Center for Craniofacial Anomalies will be studied with regard to the condition and functioning of certain facial and masticatory muscles. Electromyographic recordings will be obtained at different stages before, during and after treatment. Norms for evaluating the neuromuscular behavior are obtained from EMG recordings of 60 patients with normal skull and facial structures. EMG findings will be correlated with craniofacial morphology and with treatment.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$83,013

4.0092, RESEARCH PROGRAM ON DYNAMICS OF SPEECH ARTICULATION

K.S. Harris, Haskins Lab. Inc., *270 Crown St., New Haven, Connecticut* 06510 (P01 NS 13617-17)

This program is aimed at the analysis of the articulatory movement, particularly during normal speech production. The articulators to be examined include larynx, velopharyngeal mechanism, tongue, mandible, and lips. Techniques to be used include cinefluorography, quantitative electromyography, and acoustic analysis.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Neurological & Communicative Dis. & Stroke	$221,635

4.0093, PHOTOGNATHOGRAPHICS AS A DIAGNOSTIC METHOD IN TEMPOROMANDIBULAR DYSFUNCTION

E. Martinez Ross, Grupo de Estudio sobre Occlusion F A C T A, *Ezequiel Montes 92, Mexico City 4, D.F., Mexico*

Making a double-blind investigation one group examined 51 patients with a special clinical history and mounted models on semiadjustable 'Articulators' (Whir-mix) and another group photognathographed the same patients to prove that this method is a valuable adjunct as a diagnostic tool in determining temporomandibular dysfunction.

Photognathographics consists of exposing with a luminous beam fixed to the mandible in motion, the static film of a camera placed with its opened diaphragm at a constant and repeatable distance in dark room.

CONCLUSIONS: 62.5 percent of the diagnosed cases with the clinical history were also diagnosed with photognathographs. Further investigations will follow.

SUPPORTED BY

Grupo de Estudio sobre Occlusion F A C T A	funds n.a.

DIAGNOSIS & TREATMENT - OSTEOGENESIS

4.0094, MECHANICAL AND ELECTRICAL EFFECTS ON OSTEOGENESIS

G.A. Rodan, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Oral Biology, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 04327-04)

The long-term goal of the study is to understand, at the cellular level, the effects of mechanical and electrical stimuli on bone growth and remodeling. The objective of the next project period is to characterize the mechanical/electrical effects on the proliferation of bone and cartilage cells with respect to cellular specificity and stimulus transduction mechanism.

The working hypothesis is that the effect of the physical stimuli (1) depends on the responsive cell (state of differentiation, cell cycle stage) and (2) is mediated by a membrane perturbation translated ino a cellular message (membrane depolarization, calcium, cyclic nucleotides).

Mechanical and electrical perturbations of physiological magnitude will be applied, quantitatively, to: (1) long bones (organ explants), (2) proliferative and hypertrophying epiphyseal cartilage cells in primary and later cultures, (3) calvaria cells, periosteal and endosteal, primary and later cultures, (4) chondrosarcoma and its clones, (5) osteosarcoma and its clones, and (6) synchronized populations of the above. The following parameters will be measured: (1) to estimate proliferation: cell counts, 3H-thymidine incorporation into DNA, number of mitoses and fraction of labeled mitoses; (2) to investigate stimulus transduction: cyclic nucleotide levels, calcium, sodium and potassium tracer uptake and release from cells. The relationship between parameters (1) and (2) and the effects of experimental manipulations (drugs, etc.) on this relationship will be examined.

The accumulated knowledge should contribute to the efficient utilization of mechanical and electrical stimuli in the treatment of hard tissue defects including: craniofacial anomalies, bone loss in periodontal disease, bone fractures and related disorders.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$93,142

4.0095, OSSEOUS HEALING IN RIDGE AUGMENTATION PROCEDURES

R.J. Fonseca, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Oral Surgery, *Chapel Hill, North Carolina* 27514 (R01 DE 04918-02)

The overall objective of this study is to compare various methods of bone grafting in suitable atrophic edentulous mandibular ridges. The osseous repair and revascularization of various grafting techniques will be studied by quantitative and qualitative methods in order to select an appropriate graft system.

Adult cynomolgus monkeys will be used as the experimental animal model. Mandibular ridge augmentation procedures will be performed on edentulous monkeys. The fate of the bone grafts will be studied using clinical radiographic, microangiographic, and histologic techniques.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$49,392

4.0096, PROTEOLIPIDS AND MINERALIZATION OF BONES AND TEETH

B.D. Boyan Salyers, University of Texas, Health Science Center at Houston, Dental Branch, Dept. of Microbiology, *6515 Freeman, Houston, Texas* 77025 (R01 DE 04919-02)

The purpose of this research is to examine the role of proteolipid (hydrophobic protein complexed with acidic phospholipids) in biologic calcification. By applying techniques developed in the study of microbial calcification to vertebrate systems, the proteolipid dependency of vertebrate calcification will be established.

To resolve the dilemma that although proteolipids are normal constituents of biologic membranes, not all tissues calcify, the following approach is proposed. Calcifiability of proteolipid from calcifying tissues, tissues with a potential for ectopic calcification, ectopic deposits and tissues not known to calcify will be determined. How proteolipids capable of nucleating biologic apatite formation differ from those which are non-calcifiable will be examined by comparative characterization. The interaction of proteolipid with other tissue components during mineralization will be evaluated by studies on progressive calcification of cartilage and experimental rickets.

BIBLIOGRAPHIC REFERENCES: Boyan-Salyers, B.D. and O'Neill, P.A., Proteolipid in Biologic Calcification: An Immunochemical Study, Orthopaedic Transactions, 1978 (abstract). Ennever, J., Riggan, L., Vogel, J. and Boyan-Salyers, B., Characterization of Bacterionema matruchotii Calcification Nucleator, J. Dent. Res. 57:637-642, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$26,895

4.0097, PROTEIN-CRYSTAL RELATIONSHIPS IN MINERALIZED TISSUES

J.D. Termine, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Molecular Structure Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00074-07 LBS)

For summary: see 2.0077.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$69,936

4.0098, BIOLOGY & AGEING OF CARTILAGE

P. Person, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Research Laboratory Oral Metabolism, *800 Poly Pl., Brooklyn, New York* 11209 (527-004-P)

A. A two part study of 'Partial Regeneration of the Above-Elbow Amputated Rat Forelimb' is complete. First, it has been shown that the (100 gm male, above-elbow-amputate) rat possesses significant innate regeneration capacity leading to the restoration of the distal humeral metaphysis and a cartiliginous condyle-like extremity. Second, it has been shown that the reported induction of forelimb regeneration in the rat by indwelling electrode stimulation (R.O. Becker, Nature, 235:109-111, 1972) may be influenced by its mechanical as well as its current and voltage characteristics. B. We have also duplicated the study of Umanski and Kudokotzov (Comp. Rend. Acad. Sc. URSS 86:437-441, 1952) who reported extensive regeneration (restitution of radius and ulna) in the above-elbow-amputated neonatal rat by administration of parathyroid extract (PTE). Preliminary gross examination of limb specimens indicates that PTE did not evoke the reported responses in the present experiments. Microscopic examination for a final conclusion is now in progress. C. 'The Aerobic Metabolism of Chick Embryo Limb Bud Cartilage in Tissue Culture'. To understand the relationship of oxidative metabolism to the biosynthesis of cartilage tissue components, a preliminary study is under way in which limb buds from 108 hour old embryos are dissociated by trypsin and cultured in Earle's medium to which is added horse and fetal calf serum and chick embryo extract. At time intervals up to 20 days following initiation of cultures, homogenates are prepared and the following enzymes are assayed: Cytochrome oxidase, malic and lactic dehydrogenases and acid and alkaline phosphatases. Correlative light, scanning and transmission EM studies are also being made. 1) Person et al, Partial Regeneration of the Above-Elbow Amputated Rat Forelimb I. 2) Libbin et al. Part. Regen. of Above-Elbow Amp. Rat Forelimb. II In Press J. Morphol.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

4.0099, EFFECTS OF PARATHYROID HORMONE LEVELS ON RADIONUCLIDE IMAGING OF BONE

D.A. Garcia, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *1400 Vet. of Foreign Wars Pkwy, West Roxbury, Massachusetts* 02132 (690-004-F)

The objective of this study was to determine whether the high skeletal uptake of bone-seeking radionuclides observed in patients with hyperparathyroidism was due to abnormalities in bone formation and/or resorption.

A rat model was used to measure the partitioning of Tc-99m polyphosphate (Tc-PP) between the two bone remodelling processes, and experimental hyperparathyroidism was simulated by either the administration of parathyroid extract (PTE) or through the use of calcium-deficient diets.

The leg muscles of albino rats were implanted with two preparations: demineralized allogeneic bone matrix, a bone forming system, and devitalized autogenous bone, a resorbing system. After 3 weeks, one group of rats was injected with 200 IU PTE/Kg/day, a second group was placed on a calcium-free diet, and a third group served as controls. At six weeks, all rats were injected with Tc-PP, and the implants were removed, weighed, measured for Tc-99m activity and then ashed.

The ash data revealed that bone formation was inhibited in PTE and diet treated rats by 13 and 21 percent, respectively, relative to controls, while the resorbing process was unaffected by either treatment. There were no significant differences in Tc-99m uptake per wet gram of either type implant among the three rat groups. It was concluded that the degree of inhibition of the two remodelling processes induced in the rat model were insufficient to alter the uptake patterns of Tc-pp.

The preliminary results of this study were reported at the annual meeting of the International Association for Dental Research, March, 1976.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

V. CLEFT LIP/CLEFT PALATE

EPIDEMIOLOGY

5.0001, DIFFERENTIATION OF ORAL EPITHELIUM

A.I. Farbman, Northwestern University, Chicago Campus, School of Medicine, Dept. of Anatomy, *303 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 03934-05)

A tissue is said to differentiated when it has begun to synthesize characteristic macromolecules characteristic for that tissue. In some tissues, specific proteins have been well characterized, and their appearance during histodifferentiation can be monitored and assayed in minute quantities. In keratinizing epithelium the appearance of constitutive proteins during differentiation has been monitored in epidermis but not in oral epithelium. In this proposal, we plan to isolate and purify two low molecular weight, sulfur-rich proteins previously identified in rat lingual epithelium. When the proteins are obtained in relatively pure form, we shall raise antibodies to them, and by immunocytochemical techniques, seek to determine with what structural components of the cell they are associated. Furthermore, we shall attempt to determine whether these proteins are antigenically similar to proteins found in other stratified squamous epithelia of rats as well as of other mammals. These data will contribute to an understanding of the correlation between structure and biochemistry of oral epithelium. Moreover, they could form the basis for a biochemical classification of normal and pathological tissues.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$77,434

5.0002, WORKSHOP ON THE ETIOLOGY OF FACIAL CLEFTING

D. Bixler, Indiana University, Indiana University - Purdue University at Indianapolis, School of Dentistry, Dept. of Oral Facial Genetics, *1121 W. Michigan St., Indianapolis, Indiana* 46202 (R13 DE 05213-01)

This proposal requests support for a 3-day workshop on the etiology of facial clefting. The meeting place will be the Airlie House in Virginia and participants will be invited. A panel of experts in the fields of teratology and embryology, genetics and mathematics and epidemiology will be presenting formal papers critically reviewing the current status of the literature with regard to clefts in animals and humans. The emphasis is, however, heavily on the human data. Discussants of each formal presentation will be assigned and the entire workshop discussions and papers tape-recoded. The major topic areas to be considered are: (1) animal model systems (2) human population data (3) mathematical models applied to the etiology of clefts and (4) genetic and phenotypic markers related to clefting. The workshop will conclude with committee reports from each of these areas, and the entire group will make specific recommendations regarding the goals of future research in this area.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

ETIOLOGY - CRANIOFACIAL GROWTH

5.0003, INDUCE ORAL FACIAL MALFORMATIONS IN THE RHESUS MONKEY

H.M. McClure, Emory University, Yerkes Regional Primate Research Center, *1364 Clifton Rd. N.E., Atlanta, Georgia* 30322 (N01DE52452 (CONTRACT))

The Contractor will conduct investigations pertaining to experimental induction of oral facial malformations in fetal rhesus monkeys; documentation of metabolism of administered drugs in pregnant animals and their detuses; and chromosomalevalution of pregnant animals and products of conception, following drug administration. He will establish a breeding colony of rhesus monkeys sufficient to provide 15 pregnancies; establish the menstrual cycles of the females and conducta breeding program to insure a minimum of 15 timed pregnancies; administer specified compounds to the pregnant animals at various stages of gestation; and monitor effects of drug administration in both pregnant animals and their progeny.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$57,800

V. CLEFT LIP/CLEFT PALATE

5.0004, DIAGNOSTIC AND PROGNOSTIC TECHNIQUES IN CLEFT PALATE - THE MAXILLOFACIAL GROWTH PROJECT

H.L. Morris, University of Iowa, School of Medicine, Dept. of Otolaryngology & Maxillofacial Surgery, *Jessup Hall, Iowa City, Iowa* 52240 (P01 DE 00853-220002)

A program of experimentation involves maxillofacial growth studies in animal subjects. Objectives include elucidation of normal and abnormal growth mechanisms which may operate in human patients having craniofacial developmental anomalies. Emphasis is on identification of physical variables in cleft lip and palate habilitation which may play roles in aberrant modification of post-treatment growth and function. Recent attention has focused on the normal contraction phase of surgical wound healing in palatal mucoperiosteum and on the possible interrelationships with postsurgical maxillofacial growth.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $165,028

5.0005, MANDIBULAR MORPHOGENESIS - EMBRYONIC, NEONATAL AND POSTNATAL DEVELOPMENT

H.C. Slavkin, University of Southern California, School of Dentistry, Dept. of Biochemistry, *3551 University Ave., Los Angeles, California* 90007 (P01 DE 02848-090003)

The purpose of this subprogram is to accurately describe mandibular morphogenesis within several highly inbred strains of mice known to be either resistant or susceptible to steroid-induced congenital craniofacial malformations. Initial studies employ classical morphology including light and transmission microscopy as well as scanning electron microscopy. These studies carefully describe the genesis of the mandible starting soon after implantation of the blastocyst and the initial formation of the branchial arches through the Embryonic Period of development. We assume, further, that the principles of mandibular morphogenesis are very analogous to those operant during anterior limb morphogenesis (i.e. chondrogenesis, fibrogenesis, myogenesis and osteogenesis). Studies employ morphology, teratology and immunogenetics. Following 'baseline' studies regarding mandibular morphogenesis, we plan a series of teratological studies using congenic strains of mice (H-2a and H-2b). We also plan a series of in vitro organ culture studies attempting to determine the sites of susceptibility associated with mandibular deformities and malformations. These studies are highly original in that this information, albeit essentially descriptive, is not available in the literature, and is extremely important in subsequent understandings of mandibular abnormalities.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $66,215

5.0006, THE NATURAL HISTORY OF CLEFT LIP AND PALATE - TYPE AND FREQUENCY OF MALOCCLUSION IN CLEFTS (CL/P)

H. Aduss, University of Illinois, Medical Center at Chicago, Abraham Lincoln School of Medicine, *1853 W. Polk St., Box 6998, Chicago, Illinois* 60680 (P01 DE 02872-100036)

While the literature is relatively complete regarding the prevalence of malocclusion in the noncleft population, there is a paucity of descriptive information on malocclusion in CL/P. This is particularly true of longitudinal studies which would define the apparent increased complexity of the malocclusion from the primary to the permanent dentition. Cumulative dental cases on patients in the longitudinal series are under continuous review. Criteria for selection include: a complete series of dental casts for the primary, mixed and permanent dentitions; a specific cleft type: cleft lip only, cleft palate only, complete unilateral cleft lip and palate, and complete bilateral cleft lip and palate.

For each case the following are recorded: sex type and extent of cleft; age at lip repair; type of lip repair; age at palatal repair, type of palatal repair, name of surgeon. Each set of casts was coded for molar occlusion, overbite, overjet, and crossbite occlusion (according to individual teeth).

To analyze the longitudinal changes, the following statistical tests will be employed: a two-way analysis of variance with unequal cell numbers, a repeated measurement analysis of variance; and a one-way analysis of variance. (Major aspects study completed.)

Utilizing these data, we are now comparing our results with those recently published from Denmark where vomer flaps were used as a matter of routine. Since this operation was not employed in our series, we shall be testing the hypothesis advanced by Pruzansky and later tested by Friede: that the vomer flap is detrimental to midface growth.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$4,521

5.0007, THE NATURAL HISTORY OF CLEFT LIP AND PALATE - III, A QUANTITATIVE ANALYSIS OF THE MAXILLARY ARCH IN CL/P

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The dimensions and properties of the dental arch of the noncleft population has been extensively studied. Yet, there is only a limited amount of this same basic information on individuals with CL/P. What is available on CL/P is cross-sectional. To date, no longitudinal findings have been reported. The purpose of this study is to quantify the dimensions and properties of the maxillary arch in CL/P from the primary through the permanent dentition.

The same criteria for selection of cases outlined for Project II was utilized in this study.

The variables to be studied include: individual tooth position; arch width; arch length; arch circumference; mesio-distal tooth diameters; crowding or spacing of dental units; and arch form.

The method of study involves photographing the occlusal surface of each maxillary cast (on which anatomic landmarks had been previously labelled), projecting a photographic image on a Vanguard motion analyzer, digitization and storage of the landmarks as X-Y coordinates, and computation.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$4,521

5.0008, BIOCHEMISTRY

C. Kaye, University of Illinois, Medical Center at Chicago, Abraham Lincoln School of Medicine, Dept. of Pediatrics, *1853 W. Polk St., Box 6998, Chicago, Illinois* 60680 (P01 DE 02872-100054)

Glycosaminoglycan (GAG) Metabolism in the Pathogenesis of Vitamin Induced Cleft Palate in rats. A. Objectives and approach: 1. description of changes in glycosaminoglycan profile in development of the fetal rat palate; 2. alterations in GAG profile after treatment with Vitamin A. B. Progress: 1. GAGs increase quantitatively during palate closure; 2. GAGs, perhaps specifically hyaluronic acid (HA), are reduced in palate after Vitamin A treatment. C. Plans: 1. confirm above; 2. study GAG synthesis and degradation using radioactive precursors; 3. study specific enzymes of GAG metabolism.

Glycosaminoglycan Metabolism in Apert Syndrome (ACS) A. Objectives and approach: to determine if GAGs are increased in tissues, cells of ACS patients by quantitation of palatal and cellular GAGs, studies with radioactive precursors. B. Progress: palatal GAGs are increased 2-3 fold in ACS; fibroblast GAGs also appear to be increased. C. Plans: completion of fibroblast and precursor studies, relation of specific enzyme studies.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$8,319

5.0009, PATTERN PROFILES IN CLEFT LIP AND/OR PALATE

D.J. Dijkman, University of Michigan, Ann Arbor Campus, Center for Human Growth & Development, *Ann Arbor, Michigan* 48104 (R01 DE 04253-03)

Our objectives in this study are to identify morphologic characteristics which consistently are associated with cleft lip and/or palate probands and to test such features for occurrence in immediate family members. We will use an extensive set of data on families having a set of twins at least one of whom has a cleft lip and/or palate. We plan to (1) study probands in the data set to find characteristics consistently associated with oral clefts, (2) study co-twins, sibs, and parents for the associated characteristics to help define 'carrier' status, (3) look for patterns of occurrence of the associated characteristics in the cleft palate twin families to suggest and test possible models of inheritance, and (4) to validate our results from the twin data set by utilizing data from the Cleft Palate Clinic.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

ETIOLOGY - EMBRYOLOGY

5.0010, NORMAL AND ABNORMAL EMBRYONIC FACIAL DEVELOPMENT

M.C. Johnston, University of North Carolina, Chapel Hill Campus, Dental Research Center, Dept. of Orthodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130172)

The objectives of these studies are to determine the mechanisms involved in normal and abnormal facial development. Major emphasis is placed on development of the primary palate and cleft lip formation. Mouse and chick embryos are most commonly used with developmental changes being assessed by morphological (e.g., light and electron microscopy, autoradiography and histochemistry), biochemical and other procedures. Interactions between genetic and environmental factors in cleft lip formation is studied with A/J and C57Bl/6J mouse strains and (Phenytoin, Dilantin) and other teratogens thought to be significant in the etiology of human cleft lip. Studies on the formation, migration and differentiation of cranial neural crest also are conducted on chick and rat embryos.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $78,023

5.0011, TISSUE INTERACTION IN PALATAL SHELF CLOSURE

L.L. Brinkley, University of Michigan, Ann Arbor Campus, Medical School, Dept. of Anatomy, *1335 E. Catherine St., Ann Arbor, Michigan* 48104 (R01 DE 02774-11)

Cellular activities occurring during the course if in vitro palate closure are being studied using a circulating, submerged organ culture system. Results of studies of uptake of 3H-thymidine, -uridine and -leucine are being analyzed. Further studies monitoring the uptake of 35S-sulfate and 3H-proline will be conducted. Correlations of cell activities with the degree of palate closure will be made. Following analyses of these data and identification of peak periods of cellular activity, specific inhibitory substances will be employed to determine if these activities play a role in palate closure.

BIBLIOGRAPHIC REFERENCES: Brinkley, L., G. Basehoar, and J. Avery. Effects of craniofacial structures on mouse palatal closure in vitro. J. Dent. Res 57: 402-411 (1978).

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $85,221

5.0012, DEVELOPMENT OF THE PALATE AND LIP

B.E. Walker, Michigan State University, School of Human Medicine, Dept. of Anatomy, *Soil Science Bldg., East Lansing, Michigan* 48824 (R01 DE 02852-10)

Palate development in mice is being studied by releasing the fetus from the uterus and membranes into a fluid medium without severing the umbilical cord. Fetal movements are timed after administration of a variety of cleft palate teratogens to see whether the latter have affected functioning of the fetal neuromuscular system in a manner measurable by this technique. Excision of the fetal tongue is performed to test the ability of palatine shelves to fuse after this obstacle has been removed. The morphology of fusion under such conditions is being compared to in utero fusion, using transmission electron microscopy.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

5.0013, CHROMATIN-GLUCOCORTICOID INFLUENCES IN CLEFT PALATE

I. Bekhor, University of Southern California, School of Dentistry, Dept. of Biochemistry & Nutrition/Basic Sciences, *3551 University Ave., Los Angeles, California* 90007 (R01 DE 04031-05)

The induction of cleft palates in A/J mice in response to the administration of a glucocorticoid offers an unusual laboratory model for studies on birth defects. Our hypothesis is that the genome is involved, and experiments are proposed to assay for various aspects of the genomic structure and function. The methods call for the isolation of nuclei and cytosol from maxillary processes both from the normal and triamcinolone acetonide (TAC) injected A/J mouse embryos, for the qualitative analysis of soluble cytoplasmic proteins, for the isolation and characterization of poly(A)-messenger RNA, for determining the number of genes affected, and for studies on transcription and the involvement of chromosomal proteins in executing the adverse genetic effects observed in clefting.

Our objectives include studies on the distribution of labeled TAC chromatin to ascertain the various binding sites for labeled TAC both in active and inactive genes. Also we have isolated a fraction of chromosomal proteins which appears to be involved in binding to specific gene sequences which may be responsible for cell specialization. We are attempting to find out whether there is a linkage in binding TAC to chromatin and this fraction of chromosomal proteins. Such data will aid in understanding as to how clefting may occur in A/J mice in response to the exposure to teratogens, and may aid in the final analysis as to how teratogens may influence development of the human embryo.

BIBLIOGRAPHIC REFERENCES: Simple Isolation of DNA Hydrophobically Complexed with Presumed Gene Regulatory Proteins (M3). Bekhor, I., and Mirell, C.J. (1979). Biochemistry, in press (Feb. 20, 1979 issue). DNA Sequence Selection by Tightly-Bound Nonhistone Chromosomal Proteins. Gates, D., and Bekhor, I. (1979). Nucleic Acids Res., in press (March, 1979).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$85,489

5.0014, CONTRACTILE PROTEINS IN NORMAL PALATE MORPHOGENESIS

W.S. Krawczyk, Harvard University, Boston Campus, School of Dentistry, Dept. of Oral Biology & Pathophysiology, *188 Longwood Ave., Boston, Massachusetts* 02115 (R01 DE 04380-03)

Continuing investigations will be concerned with: (1) Further investigation on the sequential distribution of cytoplasmic actin and myosin with indirect immunofluorescent techniques in nonmuscle cells of the developing palatal shelf. Specifically, we will be interested in obtaining an accurate impression on the intensity of the immunofluorescent reaction during and subsequent to palatal shelf rotation. (2) In vitro studies investigating the effects of smooth muscle contracting agents, plus the effects of complement and the prostaglandins on epithelial and mesenchymal cells of excised palatal shelfs.

BIBLIOGRAPHIC REFERENCES: Immunofluorescence of anti-actin in gingival epthelium. David Goteiner, Walter S. Krawczyk and David G. Gillon. 1977. J. Periodontal Res. 12:436-443.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

5.0015, HUMAN PALATAL DEVELOPMENT - A STUDY OF EPITHELIAL FUSION

S.M. Meller, Harvard University, Boston Campus, School of Medicine, Dept. of Anatomy, *25 Shattuck St., Boston, Massachusetts* 02115 (R01 DE 04695-03)

The ultrastructural features of embryonic human and rodent palatal epithelium are being investigated in an attempt to become familiar with the details of secondary palate formation. Scanning electron, transmission electron, and light microscopy are being conducted on all stages of palatal tissues from 5 weeks to 12 weeks (post-fertilization) in the human.

In addition, histochemical studies principally aimed at an examination of surface coats and glycoprotein synthesis in the palatal epithelium, are being conducted. Emphasis is placed on those stages of palate development just prior to fusion in an effort to determine the mechanism of epithelial-epithelial adherence.

An in vitro system for studying human palatal development is being developed so that experimental manipulation (incorporation of labeled precursors, exposure to teratogens) may be conducted.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

5.0016, FOLATE DEFICIENCY AND IN VITRO PALATOGENESIS

D.P. DePaola, Fairleigh Dickinson University, Teaneck Hackensack Campus, School of Dentistry, Dept. of Pharmacology, *Teaneck, New Jersey* 07666 (R01 DE 05301-02)

This study is concerned with the systematic investigation of the molecular mechanisms by which folate deficiency interferes with normal orofacial development and growth. Rabbit palates will be cultured under conditions of folate deficiency induced by the use of the folate antagonist methotrexate, enzymatically by the use of Carboxypeptidase-G1, or through the use of folate deficient media. Dihydrofolate reductase activity, folate pools, nucleic acid and protein synthesis will be measured in experimental and control tissues. The distribution of 3H-MTX as well as the intracellular localization of dihydrofolate reductase will also be determined. All biochemical parameters will be correlated with morphological observations (macroscopic, microscopic including mitotic indices and ultrastructural). Correlation of morphological changes with underlying molecular mechanisms, under the controlled in vitro conditions, in a known target tissue of folic acid deficiency teratogenesis, will clearly define specific sites and mechanisms of teratogenic action involved in folate deficiency orofacial dysgenesis. This investigation would enhance present knowledge of how and at what stages in the developmental process altered control mechanisms exert their influence, and would be of considerable significance in future studies directed toward the elucidation of those factors responsible for formation of cleft palates.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $57,618

5.0017, FACIAL DEVELOPMENT, MAXILLARY PROCESS AND CLEFT PALATE

K.K. Sulik, Georgetown University, School of Medicine, Dept. of Anatomy, *3800 Reservoir Rd. N.W., Washington, District of Columbia* 20007 (R23 DE 05342-01)

The proposed complementary studies of normal and abnormal development are centered on the role of the maxillary process in primary and secondary palatal development and in developmental alterations leading to cleft palate (CP). Of the many environmental agents which can induce CP in experimental animals, vitamin A seems to have the most human relevance. Studies by the applicant have shown that alterations in dietary levels of vitamin A strikingly affect the frequency of CP in genetically susceptible mouse embryos. Work by the applicant and others indicates that vitamin A has a major effect on migrating cells and preliminary investigations indicate that extensive cellular migrations are involved in maxillary process formation. The proposed study utilizes the increasing understanding of the biochemical mechanism of action of vitamin A to analyze its teratogenicity. The conspicious maxillary deficiency produced by vitamin A in susceptible mouse strains is very similar to the oel mouse, a strain with a recessively inherited maxillary deficiency syndrome resembling Treacher Collins Syndrome. The manner in which the medial nasal process interacts with the lateral nasal and maxillary processes in primary palate formation is poorly understood. In a separate study in which diphenylhydantoin (DPH, Dilantin) is being used to produce cleft lip, lateral nasal process development is severely retarded. The interaction of deficient processes in embryos treated with either vitamin A or DPH will be compared. These experimental manipulations, should provide considerable information about the mechanisms involved in primary palate development. Scanning electron microscopy (SEM) will be used for detailed examination of morphological changes that occur in normally and abnormally developing embryos and fetuses. The majority of studies will be conducted using mouse models, though chick and subhuman primates will be studied so that comparisons may be made. The proposed morphological, histochemical, and autoradiographic study of vitamin A-induced developmental disturbances promises to provide an important link in understanding the relationship between genetic and environmental influences, specific cellular abnormalities, and facial malformations.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $33,664

5.0018, CHARACTERIZATION OF EARLY PRIMARY PALATE FORMATION

M.E. Smuts, Wheaton College, Undergraduate School, Dept. of Biology, *Norton*, *Massachusetts* 02766 (R23 DE 05368-02)

In the early development of the mammalian face, the most prominent features are the nasal placodes. The placodes participate in formation of the lateral and medial processes which, in turn, contribute to the formation of the nasal pits and the primary palate.

My previous work indicated that the placodal invaginations shaped the nasal pits and positioned the nasal processes for the alignment and contact necessary for closure of the primary palate. Since contact and adhesions in other systems appear to be mediated by surface coat material, this study investigated the alteration in surface coat material during placodal organization. Results of the biochemical comparison of fucose and glucosamine incorporation between placodal and lonplacodal facial epithelia demonstrate that the placodal epithelium accumulates these sugars in its membranes and sugar coat material.

This finding suggests that placodal cells are undergoing differentiation, expressed by morphological shape changes, reduction in DNA synthesis, as well as, synthesis of surface associated macromolecules. A cleft of the primary palate may be due to abnormal cell surface alterations on the placodes or nonalignment of the contacting nasal processes; this study is investigating both possibilities.

BIBLIOGRAPHIC REFERENCES: Hubbs, and Smute, M.S. 1978. Surface Labeling Differences between Placodal and Nonplacodal Epithelia. J. Cell Biol. 79:47a. Smuts, M.B., Hilfer, S.R. and Searls, R.L. 1978. Patterns of Cellular Proliferation During Thyroid Organogenesis. J. Embryol. Exp. Morph. 48:269-286.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $29,366

5.0019, CELLULAR PROLIFERATION AND DIFFERENTIATION DURING CRANIOFACIAL DEVELOPMENT

R.M. Pratt, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Craniofacial Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00149-05 DB)

For summary: see 4.0021.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $77,376

5.0020, THE CONTROL OF EPITHELIAL ADHESION BETWEEN PALATAL PROCESSES IN VITRO

P.R. Morgan, University of London, London Hospital Medical College, Dept. of Oral Pathology, *Turner St., London E1 2AD, England, United Kingdom*

The broad aim is to assess the relative contributions of desmosomes and extracellular glycoprotein to palatal adhesion in rodent fetuses, particular attention being given to the nature of the first-formed adhesion sites. Initial experiments were designed to determine the speed of adhesion between palatal processes explanted together in vitro. These were examined ultrastructurally for the presence of midline desmosomes and early results indicated that adhesion under these conditions is rapid, desmosomes forming within 1 hour of explantation. This approach or using short-duration organ culture methods is currently being extended to assess the effects of gestational age and teratogenic agents upon both the adhesion time and frequency of desmosome formation. The ability of other fetal oral tissues to adhere with each other and with palatal processes under the same conditions is also under investigation.

SUPPORTED BY

University of London funds n.a.

ETIOLOGY - TERATOLOGY

5.0021, THE EFFECT OF CHEMICAL MODIFICATION OF DIPHENYLHYDANTOIN ON ITS TOXICITY

B. Bhooshan, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Heart Lung & Blood Inst., Drug Tissue Interaction Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 HL 00840-03 LCP)

Seven analogues of diphenylhydantoin (DPH) synthesized during the last two years, were tested for their capactiy to induce cleft palate and cleft lip in two species of mice. All analogues of DPH except monomethylphenyl analog of DPH induced a high incidence of cleft palate and cleft lip in NIH strain or A/JAX mice. All analogues of DPH, except the dihalo derivatives were metabolized by hydroxylation of the phenyl groups and excreted in the urine as glucuronyl conjugates in both species of mice. Even through difluro analogue is not metabolized, and excreted in the urine as unchanged drug, it induced a very high incidence of cleft palate in both species. This finding indicates that metabolism of DPH by hydroxylation (epoxidation) pathway may not be a prerequisite for the induction of cleft palate.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Heart Lung & Blood
Inst. funds n.a.

5.0022, NEUROTRANSMITTER CONTROL OF PALATE MORPHOGENESIS (MICE)

E.F. Zimmerman, Childrens Hospital Medical Center, *3245 Burnet Ave., Cincinnati, Ohio* 45229 (P30 HD 05221-100034)

This project is part of a broader program (HD 05221-10) whose summary states: The Institute for Developmental Research (IDR) is devoted to research related to human development which may assist in finding causes and means of prevention of mental retardation or in finding means of ameliorating the effects of mental retardation. The IDR is a part of the Children's Hospital Research Foundation. By its close affiliation with many of the Children's Hospital Medical Center's Research Divisions, University Affiliated Facilities, and other hospitals and clinics the IDR, in addition to its own research program, enhances and stimulates mental retardation research in the entire Children's Hospital Medical Center and in other Departments of the University of Cincinnati College of Medicine.

V. CLEFT LIP/CLEFT PALATE

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Child Health
& Human Development funds n.a.

5.0023, SELECTED FACTORS INFLUENCING INCIDENCE OF ORAL CLEFTS

J. Niebyl, Johns Hopkins University, School of Medicine, Dept. of Obstetrics & Gynecology, *725 N. Wolfe St., Baltimore, Maryland* 21205 (N01DE62486 (CONTRACT))

A study to determine the feasibility of studying high-risk mothers (mothers who have given birth to cleft children previously) with respect to potential environmental and metabolic etiological factors affecting their children prenatally and resulting in oral clefts. The final target of such research would be to identify a large-scale high-risk group of mothers and to reduce the risk by modifying prenatal circumstances. The first step in the development of a preventive program for congenital cleft lip and palate will be to identify likely etiologic factors and explore a small population to determine the needs and objectives of a larger study.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

5.0024, STEROID RECEPTORS IN CRANIOFACIAL TERATOLOGY

H.C. Slavkin, University of Southern California, School of Dentistry, Dept. of Biochemistry, *3551 University Ave., Los Angeles, California* 90007 (P01 DE 02848-090002)

The major goal of this subprogram is to understand the mechanism by which a teratogen produces craniofacial malformations in embryonic, fetal, neonatal and postnatal development in an animal model. The abnormalities to be studied include teratogen-induced mandibular deformities, cleft lip and palate, possible vestibular dysfunctions, and major skeletal and soft tissue abnormalities. We assume that steroids and steroid-like substances provide a useful paradigm with which to study general interactions between genotype and environmental insults. Further, we assume that steroid-induced clefting is coincidental with many other malformations, especially growth retardation, and speculate that genetic susceptibility to steroid-induced clefting during pregnancy is associated with the H-2 loci in mice. Using mouse strains of different H-2 haplotype or alleles we predict that H-2a maternal influences play a significant effect upon fetal susceptibility to congenital craniofacial malformations. These studies employ classical immunogenetics, mouse genetics, steroid chemistry and experimental embryology. In addition to information obtained about the mother and father (e.g. blood studies, weight, age, treatment regimens, etc.) we also obtain critical data on the individual fetuses as well as data on the litter (e.g. size, weight, developmental 'age', gross abnormalities, histology). Computer-assisted analyses suggest, using multiple variate analyses that H-2 maternal influences provide a significant effect upon fetal morphogenesis. It is projected that these studies will enable improvements in detection of females 'at risk' and provide significant predictors by which one can follow pregnancies associated with congenital malformations.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $86,985

5.0025, TERATOGENS ON CLEFT PALATE FORMATION

E.F. Zimmerman, Childrens Hospital Medical Center, *3245 Burnet Ave., Cincinnati, Ohio* 45229 (R01 DE 03469-08)

In this continuing study of palate morphogenesis and effects of teratogens in causing cleft palate, the proposed research will be (1) to determine the distribution of neurotransmitters in the palate, (2) to correlate mesenchymal cells growing in culture with those present in situ, (3) to test the effects of neurotransmitters on morphology of cells in culture and the effects of appropriate antagonists, (4) to isolate and maintain various palatal cell types in culture, (5) to determine the presence of neurotransmitter receptors on palatal cells, (6) to look for the presence of neural antigens immunologically on surfaces of palatal cells and, (7) to determine if palatal cells elicit action potentials.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $133,668

5.0026, CLEFT PALATE - TERATOGENIC ROLE OF CORTISONE

B.J. Jacobson, Boston Biomedical Research Inst., Dept. of Fine Structure Research, *20 Staniford St., Boston, Massachusetts* 02114 (R01 DE 04507-02)

Cleft palate is one of the most prevalent congenital malformations seen in man. Corticosteroid-induced cleft palate has been the object of extensive research; however, the mechanism by which this birth defect is generated has not been firmly established. The objectives of the proposed research deal with the possible mechanism by which cortisone delays the movement of the palatine shelves, resulting in a decreased possibility for fusion and a cleft of the secondary palate. Because of the ease of detecting it and also because of its present or absent nature, this defect lends itself to many aspects of experimental teratogenesis.

Palatal shelves at various stages of embryogenesis will be isolated from normal mothers and from mothers treated with cortisone on the eleventh to fourteenth days of pregnancy. Both normal and cortisone-treated mothers will receive radioactive glucosamine 24 hrs prior to sacrifice. The content of palatal glycosaminoglycans will be determined in both normal and abnormal palatal shelves at several stages of palatogenesis. The level of certain enzymes involved in the synthesis of the palatal glycosaminoglycans will also be determined at similar stages of palatogenesis. The effect of hyaluronic acid on palatal cells in culture will be studied, in order to determine whether this glycosaminoglycan plays a role in mesenchymal cell migration and shelf fusion by virtue of a stimulation of the cells biosynthetic capacities.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$74,860

5.0027, CRANIOFACIAL ANOMALIES AND PROTEIN RECEPTORS

A.S. Goldman, Childrens Hospital of Philadelphia, Division of Teratology, *34th St. & Civic Ctr. Blvd., Philadelphia, Pennsylvania* 19104 (R01 DE 04622-03)

The major goal of this proposal is to elucidate for the first time the mode of action of a teratogen at the molecular level in both animal models and humans with congenital abnormalities. The abnormality to be studied is teratogen-induced cleft palate and the mechanism of action to be studied is the involvement of specific cytosol and nuclear receptor proteins in the corticoid induced derangement of gene action in mice. We propose to correlate the kind and amount of these receptors with the differing degree of teratogenic susceptibility to cleft palate by corticoids in different strains of mice. We also plan to determine whether other cleft palate teratogens have involvement of receptor proteins in their teratogenicity and whether these receptor proteins can be identified in children with cleft palate. Ultimately, we hope to be able to detect teratogenic vulnerability of human fetuses exposed to drugs by the receptor level in amniotic cells taken at amniocentesis.

BIBLIOGRAPHIC REFERENCES: Goldman, A.S.: Fetal trimethadione syndrome. Teratogen Update. Teratology. 17: 103-106, 1978. Saenger, P., A.S. Goldman, L.S. Levine, S. Korth-Schutz, E.C. Muecke, M. Katsumata, Y. Doberne, and M.I. New: Prepubertal diagnosis of steroid alpha-reductase deficiency. J. Clin. Endocrin. & Metabolism. 46:627-634, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$112,635

5.0028, BASIS OF DRUG-INDUCED CLEFT PALATE

D.L. Gasser, University of Pennsylvania, School of Medicine, Dept. of Human Genetics, *36th & Hamilton Walk, Philadelphia, Pennsylvania* 19174 (R01 DE 05008-01)

The research proposed in this application deals with the genetic basis of susceptibility to drug-induced cleft palate and other craniofacial anomalies such as micrognathia and agnathia. The primary emphasis is on studying the role of the major histocompatibility complex (H-2 in mice and AgB in rats) in determining susceptibility to these disorders. We propose to localize the specific gene within the mouse H-2 region which is known to affect susceptibility to cortisone-induced cleft palate. We also wish to map precisely the gene which controls the quantity of a cortisol-binding protein, and to determine whether antisera directed to antigens coded by various parts of H-2 can inhibit cortisol binding.

The effect of H-2 on sensitivity of thymus cells to corticosteroids will also be studied. We would like to determine whether the same cortisol-binding proteins that are found in fetal palates can be found in or on thymus cells, and whether this explains the H-2-linked differences in thymus cell sensitivity to corticosteroids which have been reported.

Other experiments are proposed which will explore the genetic basis of patroclinous inheritance to cleft palate susceptibility, and the possible involvement of the rat AgB locus in drug sensitivities.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$52,650

5.0029, CRANIOFACIAL ABNORMALITIES IN MICE WITH VDRR

R.J. Iorio, Marquette University, School of Dentistry, Dept. of Anatomical Sciences, *604 N. 16th St., Milwaukee, Wisconsin* 53233 (R01 DE 05024-01)

Using appropriate genetic crosses, C57BL/6J mice will be used to produce males, heterozygous females, and homozygous females affected with an X-linked dominant form of vitamin D resistant rickets (VDRR). We propose to study the development and appearance of craniofacial and dental abnormalities associated with this disease and to assess effects of therapeutic measures used in the treatment of VDRR in humans. We plan to use radiology, cephalometry, histology, histochemistry, and biochemistry to obtain our results.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$47,217

5.0030, GLUCOCORTICOID RECEPTORS AND CLEFT PALATE

J.F. Hackney, State University System of Florida, University of South Florida, School of Medicine, Dept. of Pharmacology & Therapeutics, *4202 Fowler Ave., Tampa, Florida* 33620 (R01 DE 05168-01)

Glucocorticoids cause cleft palate in mice. A glucocorticoid binding substance with receptor-like properties has been found in fetal tissue. We wish to determine whether this receptor is associated with glucocorticoid produced cleft palate. Three approaches will be used. 1) The relationship between mouse strain susceptibility and receptor interaction will be explored further. Glucocorticoid binding experiments with fetal cell supernatant have indicated no differences in amount of receptor between mouse strains. We propose that strain differences may be due to receptor accessibility in vivo. Pregnant mice will be injected either with unlabeled glucocorticoid or with vehicle alone. Fetal cell supernatant will be incubated with 3H-triamcinolone acetonide and bound radioactivity will be measured. The difference in radioactivity bound between control and glucocorticoid treated animals will indicate the amount of administered glucocorticoid bound. 2) Progestins, which do not cause cleft palate, compete with 3H-triamcinolone acetonide for the receptor in supernatant. Progestins will be tested as antagonists of cleft palate formation by glucocorticoids. They will also be tested for their ability to bind at the glucocorticoid site when administered in vivo as described in (1). 3) Fractionation of the 3H-triamcinolone acetonide-receptor complex on DEAE-agarose has revealed two peaks of bound radioactivity. We will test for any relationship between these peaks. We will also determine relative peak amounts: a) during the sensitive period of gestation; b) in mouse strains with differing cleft palate susceptibility; and c) in the presence of competing steroids. An understanding of the biochemical basis of cleft palate susceptibility in mice should provide a basis for better understanding human susceptibility to teratogens, and how these problems can be predicted and prevented.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$41,158

5.0031, DEVELOPMENT OF CARTILAGE

J.P. Pennypacker, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00253-02 DB)

For summary: see 4.0023.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$16,841

5.0032, ULTRASTRUCTURAL AND BIOCHEMICAL INVESTIGATION OF TERATOLOGICAL MECHANISMS

R.M. Shah, University of British Columbia, Faculty of Dentistry, Dept. of Oral Biology, *2075 Wesbrook Pl., Vancouver, British Columbia, Canada* V6T 1W5 (MA 6035)

The major thrust of the proposed research is to gain information about the mechanisms of normal and abnormal palatal development in hamster. The immediate objectives are to compare and contrast the sequential changes in enzymic, carbohydrate and nucleic acid histochemistry and also sequential ultrastructural appearances of 5-fluorouracil and 6-mercaptopurine induced cleft palate with those following treatment with hydrocortisone, triamcinolone and hadacidin. Also, we intend to study the metabolism of hadacidin in the maternal, placental and fetal tissues. Studies on the biochemical aspects of the hydrocortisone induced cleft palate are under progress. Glucocorticoid receptor binding sites have been isolated from the nuclear and cytosol fractions of the hamster palatal tissues and studies are in progress to chemically characterize the receptor sites. In addition, ultrastructural and histochemical analysis of normal palatogenesis in the chick embryo have lead to further understanding of important species differences and consequently different regulatory mechanisms. Studies on ultrastructural and histochemical aspects of abnormal palatal development in chick embryos are also initiated.

SUPPORTED BY

Medical Research Council of Canada	$25,000

ETIOLOGY - GENETICS

5.0033, ORAL-FACIAL VARIATIONS IN RELATIVES OF CLEFT PROBANDS

D. Bixler, Indiana University, Indiana University - Purdue University at Indianapolis, School of Dentistry, Dept. of Oral Facial Genetics, *1121 W. Michigan St., Indianapolis, Indiana* 46202 (R01 DE 03707-06)

The purpose of this research is to identify specific oral-facial variations present in the near relatives (1st and 2nd degree) of cleft lip and palate probands. This is a continuation of the project begun years ago to identify non-cleft persons with major genetic liability for transmitting the trait to offspring. We have, so far, found no significance morphologic variations but the speech functions of parents of cleft children do show an increase in velo-pharyngeal inadequacy. The significance of this finding is unknown. However, we have made a major change in our working hypothesis. Instead of studying relatives of all cleft probands for these oral-facial variations, as is compatible with the multifactorial model of causation of cleft lip and palate, we will study only relatives in multipally affected families, and only those in unilateral lines, for evidence of clefting gene action. The reason for this approach is recent observations we have made on the Danish population of clefts denies those predictions used to support multifactorial inheritance and, instead, they support the presence of monogenic, dominantly inherited form of both cleft lip and cleft palate within the heterogeneous group of all clefts. Hence, the use of multipally affected families conceivably limits the investigation to a single etiologic cleft type, the one most likely to yeild a positive result.

In this study, a series of 15-20 families with at least 2 affecteds in near relatives will be evaluated for (1) morphologic and (2) functional (speech) variations as evidence of minor expression of a monogenic trait. Such minor expressions will be most useful to the genetic counselor in providing recurrence risks for affected families.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$38,695

5.0034, GENETICS OF CELL ADHESION AND CLEFT PALATE FORMATION

M.A. Edidin, Johns Hopkins University, School of Arts & Sciences, Dept. of Biology, *34th & Charles Sts., Baltimore, Maryland* 21218 (R01 DE 04481-02)

OBJECTIVES: (1) To determine the role of the H-2 gene complex in modulating intercellular adhesion of normal embryonic fibroblasts obtained from congenic resistant mouse strains. (2) To extend objective (1) to the effect of the H-2 system upon heterotypic tissue combinations, such as epithelial-fibroblast adhesion. (3) To investigate factors that differentially affect cell-cell adhesion according to H-2 genotype. Such reagents as anti-H-2 isoantisera and neuraminidase appear to exert such a differential effect. (4) To investigate the corticosteroid induced cleft palate model in which the H-2 genotype is linked to the incidence of cleft palate formation and to learn if developmental anomalies may be due to cell surface alterations that are reflected as changes in intercellular adhesion.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$51,571

5.0035, GENETIC CONTROL OF SUSCEPTIBILITY TO CLEFT PALATE

M.L. Tyan, University of California, Los Angeles Campus, School of Medicine, Dept. of Medicine, *2025 Zonal Ave., Los Angeles, California* 90024 (R01 DE 05165-01)

Evidence suggests that an increased incidence of cleft palate may be associated with HLA-A2, a major histocompatibility complex antigen. If this is true then HLA antigens can be used as genetic markers for increased susceptibility to cleft lip and/or palate. The proposed studies have been designed to confirm the HLA/cleft palate association. Cooperating institutions throughout the Los Angeles Metropolitan area will provide subjects to be HLA typed. About 1,100 patients will be available. All HLA typing of experimental and control populations will be done by the UCLA HLA typing facility directed by Dr. P.I. Terasaki. A sample of blood containing live cells and a sample of serum from each patient will be preserved in liquid nitrogen for future use. The identification of genetic markers for cleft lip and/or palate susceptibility will lead to the development of procedures to reduce the incidence of these craniofacial anomalies.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $75,084

5.0036, AM CLEFT PALATE ASS. - ON GENETICS AND CLEFTING

L.F. Wilson Mackby, American Cleft Palate Assn., *c/o Univ. of North Carolina, Chapel Hill, North Carolina* 27514 (R13 DE 05349-01)

This grant would provide funds for a four-hour morning or afternoon panel to present and discuss the field of Genetics as it relates to clefting and other craniofacial defects. The program will include a group of essayists, a panel of discussants, audience participation and written assessment of program effectiveness.

Our objectives are as follows: 1. To describe the current understanding of the molecular and cellular biologic mechanics of inheritance and the present state of prevention of genetic disease. 2. To report studies describing genetic influence on occurrence of clefting and other craniofacial anomalies. 3. To provide a forum for discussion of implications of increasing occurrence of anomalies as a consequence of rehabilitation of affected individuals.

The following titles will be covered: 1. Molecular Biology of the Gene Cellular Biology of the Chromosome 2. Mechanisms of Human Inheritance 3. Genetics of Cleft Lip and Palate 4. Craniofacial Disorders as Part of Other Syndromes 5. Diagnostic Techniques for Identification of Defects and Counseling of patients 6. Treatment and Prevention of Genetic Disease - Present and Future 7. Ethical Issues in Treatment and Prevention of Genetic Disease

Genetic aspects of craniofacial malformations incorporate more than a discussion of risk of recurrence.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $1,680

5.0037, A GENETIC STUDY OF HUMAN OROFACIAL CLEFTS

S.W. Oka, Lancaster Cleft Palate Clinic, Genetic Services, *24 N. Lime St., Lancaster, Pennsylvania* 17602 (R23 DE 04537-03)

Family pedigree data on 1178 probands are to be analyzed from a clinical epidemiological and from a genetic orientation. A subpopulation of pedigrees with a positive family history will be focused upon for the initial analysis to test specific genetic hypotheses including the generally accepted multifactorial threshold model.

Previously collected data include dental casts, facial photographs, and cephalograms. The cephalograms which were collected by family groups will be analyzed to compare basi-cranial and C1 and C2 mensurational relationships. This analysis will seek variant patterns of these structures in unaffected relatives. It will also enable a comparison of methodology by measuring these structures from radiographs as well as directly from digitally enhanced cephalograms.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

5.0038, DEVELOPMENTAL PROCESSES IN GENETICALLY CONTROLLED MALFORMATIONS

K.S. Brown, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00024-13 DB)

For summary: see 4.0030.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,

National Inst. of Health,
National Inst. of Dental
Research $110,689

5.0039, STUDIES ON HLA AND SUSCEPTIBILITY TO CLEFT LIP/PALATE

M.L. Tyan, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Intermediate Care & Geriatrics Medicine Section, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-002-P)

Present evidence suggests that an increased incidence of cleft palate is associated with HLA-A2, a major histocompatibility complex antigen. If this is true then the HLA antigens can be used as genetic markers for the increased risk for cleft lip and/or cleft palate. The proposed studies have been designed to confirm the HLA/cleft palate association. Cooperating institutions throughout the Los Angeles Metropolitan area will provide the subjects to be HLA typed. About 1,100 patients will be available. All typing of experimental and control populations will be done by Dr. Terasaki's Laboratory at UCLA. A sample containing live cells and a sample of serum from each patient will be preserved in liquid nitrogen for future experimentation. Future tests will depend on the outcome of animal experiments in progress. The identification of genetic markers for cleft lip and/or cleft palate susceptibility is necessary for the development of procedures to reduce the incidence of the craniofacial anomaly.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

PATHOLOGY - SPEECH

5.0040, DIAGNOSTIC AND PROGNOSTIC TECHNIQUES IN CLEFT PALATE - THE SPEECH PATHOLOGY PROJECT

H.L. Morris, University of Iowa, School of Medicine, Dept. of Otolaryngology & Maxillofacial Surgery, *Jessup Hall, Iowa City, Iowa* 52240 (P01 DE 00853-220001)

The purpose of the speech pathology project is to investigate the articulatory skills of our longitudinal sample in respect to differential diagnosis of velopharyngeal closure and the predictive value of articulation tests. Additional studies will investigate the heterogeneity of various subgroups of cleft palate individuals to provide a normative sample for which future comparisons can be made. Prediction of velopharyngeal closure will be studied by examining variables such as type of cleft, age at surgery, type of surgery and cinefluorographic results.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $43,428

5.0041, DIAGNOSTIC AND PROGNOSTIC TECHNIQUES IN CLEFT PALATE - THE SPEECH PHYSIOLOGY AND ANATOMY PROJECT

H.L. Morris, University of Iowa, School of Medicine, Dept. of Otolaryngology & Maxillofacial Surgery, *Jessup Hall, Iowa City, Iowa* 52240 (P01 DE 00853-220003)

The general purpose of the Speech Physiology and Anatomy Project is to provide additional information concerning the structure and function of the velopharyngeal (VP) mechanism both in normals and in cleft palate individuals. It is expected that this information will lead to improved treatment procedures for speech communication purposes in cleft palate patients. Since the ultimate goal in cleft palate management for speech purposes is to provide the patient with a functionally adequate VP mechanism, a thorough understanding of the normal non-cleft mechanism is essential in establishing an emulative model. Therefore, the investigative strategy will include study of a limited number of normal as well as cleft palate subjects. Procedures to be used include anatomical dissection and histological sectioning, radiographic films (of several types), electromyography (EMG), endoscopy, and air pressure and flow.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $117,256

5.0042, SPEECH AND HEARING TESTING AND RESEARCH UNIT

S.J. Peterson Falzone, University of Illinois, Medical Center at Chicago, Abraham Lincoln School of Medicine, Dept. of Otolaryngology, *1853 W. Polk St., Box 6998, Chicago, Illinois* 60680 (P01 DE 02872-100057)

Current studies are designed to expand our documentation of the effect of specific craniofacial anomalies on hearing, speech and language development. The major thrust of research in auditory function is in development of the brainstem electric response in infants with clefts and other malformations of the craniofacial complex. Presence or absence of auditory processing disorders is being studied in our older children. Studies on alterations in vowel formant frequencies in anomalous supralaryngeal vocal tracts are being extended to examine durational and perceptual data. Radiographic data on Apert and Crouzon is being analyzed for relative contribution of a variety of factors to the distortions of the nasopharynx and cranial base. Laryngeal function in patients with ectodermal dysplasia and the EEC syndrome is being studied via both acoustical analysis and high-speed laryngeal photography.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $54,902

5.0043, PHYSIOLOGICAL STUDY OF SPEECH ADAPTATION

S.L. Hamlet, University of Maryland, College Park Campus, School of Business & Management, Dept. of Hearing & Speech Science, *College Park, Maryland* 20742 (R01 DE 03631-06)

The objective of the proposed research is to obtain physiological and acoustical information on the process of learning compensatory speech patterns. Procedures involve altering the oral contours by wearing experimental alveolar-palatal prostheses, similar to orthodontic bite plates. Acoustical analysis of speech will be done, and physiological measurements made of jaw motions, larynx height, timing and location of tongue-palate contact, and breath pressure and flow. Subjects will be used who have normal speech as well as those who have presently normal sounding speech, but a history of sibilant articulation defects successfully remediated by speech therapy. Data will be recorded before and at the time of prosthesis insertion, after a period of adaptation lasting one or more weeks, and again after a month during which the prosthesis is not worn. A detailed descriptive study is planned on compensatory sibilant articulation. The relationship of pre-speech jaw activity to later jaw activity during speech utterance will be studied from the perspective of planning of speech motor sequences and compensatory strategies.

BIBLIOGRAPHIC REFERENCES: Hamlet, S.L., Stone, M., Cullison, B., Schoner, L. Further observations on speech preparatory activity of the jaw. J. Acoust. Soc. Amer. 63: s33 (1978). Hamlet, S.L. Evaluation of a rectangular ultrasonic transducer for laryngeal use. J. Acoust. Soc. Amer. 64: s91 (1978).

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $49,414

5.0044, CLEFT PALATE MALOCCLUSION AND LINGUAL ARTICULATION

D.W. Warren, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Dental Ecology, *Chapel Hill, North Carolina* 27514 (R01 DE 04267-04)

The objectives of this proposed research are to: a) determine the relationship between compensatory speech patterns and aerodynamic events in cleft palate and severe malocclusion; b) determine the effects of changes in oral dimensions on oral/nasal resonance and voice quality; c) determine the effects of maxillary osteotomy on airway breathing patterns and speech; d) develop models of disordered speech based on clinical findings.

The pressure-flow technique will be used with acoustic, palatographic and preceptual approaches to document, quantify and relate physiologic, aerodynamic and acoustic events during speech. A computer based data collection and analysis system will monitor and store a variety of data simultaneously and process any combination using recent digital techniques.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $44,110

PATHOLOGY - CRANIOFACIAL GROWTH

5.0045, THE NATURAL HISTORY OF CLEFT LIP AND PALATE - I. MORPHOANALYSIS, II. GROWTH PATTERN

S. Pruzansky, University of Illinois, Medical Center at Chicago, Abraham Lincoln School of Medicine, Dept. of Pediatrics, *1853 W. Polk St., Box 6998, Chicago, Illinois* 60680 (P01 DE 02872-100035)

Given a cadre of well trained surgeons utilizing generally approved operative procedures, we hypothesized that the initial state is predictive of the subsequent state as determined by analysis of occlusion and facial skeletal development.

The initial state is determined by a number of parameters which can be categorized under the following headings: I. Morphoanalysis - based on standardized photographs, study casts and cephalometric radiographs beginning with the unoperated infant. II. Growth Patterns: Mapping and projecting such patterns is critical in treatment planning, effect of surgery, and monitoring progress. Based on this experience we hope to develop empirical data allowing for growth projection.

For each project, an initial qualitative review is conducted for purpose of determining whether specific hypotheses can be tested with available data base. This procedure is followed by development of a protocol allowing for quantitative determinations. These steps have been completed on a number of projects.

To identify predictive correlations between conditions present before surgery and subsequent facial development, canonical correlation analysis has been utilized. This test was used to determine the relationship of one set of dependent variables to another set of independent variables. A linear combination was derived from each of the sets of variables so that the correlationn between the two linear combinations was maximized. The linear combinations of the original variables were produced to account for a maximum amount of relationship between the two sets of variables.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$9,042

PATHOLOGY - AUDIOLOGY

5.0046, A NON-HUMAN PRIMATE MODEL OF CLEFT PALATE AND ITS IMPLICATIONS FOR MIDDLE EAR PATHOLOGY (ABBREV)

E.J. Forrest, University of Pittsburgh, Cleft Palate Center, *Salk Hall 313, Pittsburgh, Pennsylvania* 15261 (P01 DE 01697-170033)

The major objective of this program is to develop a rational means of eliminating middle ear pathology universally associated with cleft palate. This disorder is related to a dysfunctional Eustachian tube system, and the patency of the Eustachian tube is dependent upon the functional efficiency of the tensor veli palatini muscle and velar integrity.

APPROACH: A non-human primate model which replicates those anatomic and physiologic conditions which have been suggested as causative predispositional factors in Eustachian tube dysfunction and middle ear effusion in cleft palate populations will be created. The model will lend itself to variable control and allow for the identification of the anomaly or anomalies characteristic of cleft individuals and responsible for their middle ear effusions.

We will develop and implement those surgical procedures such as tensor veli palatini muscle transposition and alteration. These procedures will first alter the mechanism and reestablish functional integrity to eliminate the surgically created pathological condition. The developed surgical techniques will be related to and integrated with currently practiced clinical reconstructive surgery.

This work is continuing according to plan, and it has been possible, by surgical intervention in the palates of primates, to watch these animals develop middle ear effusion without direct alteration in the Eustachian tube.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$35,052

DIAGNOSIS & TREATMENT

5.0047, DIAGNOSTIC AND PROGNOSTIC TECHNIQUES IN CLEFT PALATE - THE SURGERY PROJECT

H.L. Morris, University of Iowa, School of Medicine, Dept. of Otolaryngology & Maxillofacial Surgery, *Jessup Hall, Iowa City, Iowa* 52240 (P01 DE 00853-220004)

The Surgery Project is designed to provide additional information about the effects of cleft lip and palate surgery on development of the midface. Studies proposed involve both human subjects and animal models, with a main focus of attention on questions of effects of lip surgery. A second purpose is to provide descriptive information about late results (adult) of cleft lip and palate surgery, with specific interest in secondary deformities.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$108,571

5.0048, OTITIS MEDIA AND ITS TREATMENT IN CLEFT PALATE (INFANTS)

E.J. Forrest, University of Pittsburgh, Cleft Palate Center, *Salk Hall 313, Pittsburgh, Pennsylvania* 15261 (P01 DE 01697-170020)

The primary objective of this project is to understand the natural history and short- and long-term effects of otitis media in infants with cleft palate and to help determine optimal methods of management by means of a controlled, prospective, clinical trial.

This is a longitudinal study, and infants are randomly selected and placed in groups for treatment of ear disease by myringotomy at three months, six months, or twelve months of age. If active symptoms occur, treatment is undertaken. This study is proceeding at a reasonable pace, and it appears thus far that myringotomy with insertion of polyethylene tubes can probably be safely delayed until six months of age. After that age, most infants appear to experience active ear distress. The study will continue for an additional two years.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $61,605

5.0049, TWO-DIMENSIONAL ULTRASONIC VISUALIZATION OF LATERAL PHARYNGEAL WALL MOTION DURING SPEECH AND SWALLOWING (ABBREV)

E.J. Forrest, University of Pittsburgh, Cleft Palate Center, *Salk Hall 313, Pittsburgh, Pennsylvania* 15261 (P01 DE 01697-170032)

The objective of this investigation is to see if the movements of the lateral pharyngeal walls as radiographically visualized in frontal view can be equally well seen using two-dimensional ultrasound imaging techniques, thus eliminating the frontal x-ray view. Since ultrasound uses no radiation, the total radiation dosage to the patient would be reduced by one-third.

The procedure is to develop an ultrasound head capable of depicting bilaterally the pharyngeal walls. This instrumentation is developed and functioning but needs additional improvements which are being sought at this time.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $70,103

5.0050, PREDICTING ARTICULATION FROM CINEFLUOROGRAPHIC MEASURES

R.L. Shelton, University of Arizona, School of Fine Arts, Dept. of Speech & Hearing Sciences, *Tucson, Arizona* 85721 (R01 DE 03350-09)

The proposed research is intended to evaluate treatments directed to misarticulating children and to predict treatment outcomes. Two subject categories are employed: cleft palate and functional articulation disorder. The cleft palate studies have three purposes: (1) evaluate biofeedback training directed to velopharyngeal closure, (2) evaluate the influence of oronasal fistulas on speech and response to speech training, and (3) determine what speech gains can be achieved through training by individuals with velopharyngeal closure deficits. These studies measure articulation in single subject, repeated measures research designs. Oral videoendoscopic and pressure-flow instrumentation is used for biofeedback and for assessment of velopharyngeal function.

The articulation studies are to develop and evaluate remedial speech procedures. Responses to treatment is predicted from articulation and other measures, and predictions are made through regression procedure. Also, the estimated omega squared statistic is used in group comparisons to determine variance accounted for. Study variables include articulation, language, reading, listening, psychosocial, and dental measures. The articulation studies also use clustering procedure to identify homogeneous subject subsets. Remediation is conceptualized within a perceptual-motor learning model, and response acquisition and automatization are emphasized.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $60,206

5.0051, PIN-RETAINED PROSTHESIS WITH SURGERY IN CLEFT PALATE

R.F. Hagerty, St. Francis Xavier Hospital, *135 Rutledge Ave., Charleston, South Carolina* 29401 (R01 DE 04517-01A1)

This research project is designed to evaluate the primary method of cleft lip and palate treatment. This method consists of the use of a pin-retained expandable artificial palate in conjunction with surgical procedures to restore near normal anatomy and function. Surgical procedures which might interfere with mid-facial growth, such as the elevation of mucoperiosteal flaps from the palate or vomer, are delayed until the eruption of the six year molar teeth. It is designed to encourage normal habits of eating and speech, to provide some protection from middle ear infections and to encourage normal development of facial growth and dental arch relationships.

The method of this study is to evaluate the feeding, speech, hearing, facial growth, dental arch relationships and social development of the individuals treated by this regimen. They are compared in the above categories with appropriately matched normals and conventionally treated cleft lip and palate children.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$61,154

5.0052, STUDIES OF SENSORIMOTOR IMPAIRMENTS OF THE MOUTH AND PHARYNX

J.F. Bosma, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Oral & Pharyngeal Development Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00182-04 CI)

For summary: see 4.0071.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$41,295

VI. OTHER CONGENITAL ANOMALIES & SYNDROMES

ETIOLOGY - CRANIOFACIAL GROWTH

6.0001, BIOCHEMISTRY

C. Kaye, University of Illinois, Medical Center at Chicago, Abraham Lincoln School of Medicine, Dept. of Pediatrics, *1853 W. Polk St., Box 6998, Chicago, Illinois* 60680 (P01 DE 02872-100054)

For summary: see 5.0008.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$8,318

ETIOLOGY - TERATOLOGY

6.0002, PCB AND TCDD OROFACIAL TERATOGENESIS IN M. MULATTA

W.P. McNulty, Medical Research Foundation of Oregon, Laboratory of Pathology, *6415 S.W. Canyon Ct., Portland, Oregon* 97207 (R01 DE 04333-03)

The project has two objectives. (1) We are documenting normal prenatal craniofacial morphogenesis in M. mulatta by a combination of photographic, radiologic, and histologic techniques. (2) We are investigating possible teratogenic effects of polychlorinated biphenyls (PCBs) and 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). PCBs, a stable series of chemicals widely used in industry, have become environmental pollutants of proven toxicity. Experimentally they have caused aberrant amelogenesis and dental follicle formation in young rhesus monkeys. TCDD is a contaminant in industrial compounds such as pentachlorophenol and the herbicide 2,4,5-T. It is a known teratogen for rodents, inducing cleft palate among other malformations, and has been implicated in stillbirths and human birth defects following the use of defoliants in Vietnam.

Both compounds have proven to be potent abortifacients when administered orally during weeks 4 to 6 of pregnancy at doses of 1 or micron g/kg for TCDD, and 0.6 or 3 mg/kg for 3,4,3',4'-tetrachlorobiphenyl. Fetuses which were not aborted at 0.2 or 1 microgram/kg TCDD showed abnormalities in the uvula and soft palate and in tooth formation.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$95,818

6.0003, OROFACIAL ANOMALIES IN PHENYTOIN TERATOGENESIS

A.S. Goldman, Childrens Hospital of Philadelphia, Division of Teratology, *34th St. & Civic Ctr. Blvd., Philadelphia, Pennsylvania* 19104 (R01 DE 05041-01)

We propose to confirm and extend our observations that susceptibility to phenytoin-induced cleft palate in inbred strains of mice is regulated by a gene in or near the H-2 histocompatibility locus. If so, we hypothesize that the molecular mechanism by which the hydantoins induce human cleft palate is similar to our recent observations on corticoid induced cleft palate, namely, binding of corticoids to cytosol receptors, uptake by nuclei, and activation or depression of transcription or translation. Binding of 3H-dilantin will be studied in palatal mesenchymal cells of sensitive strains of mice by conventional techniques and by our micromethods of isoelectrofocusing. Dilantin and other cleft palate teratogen receptors will also be sought in palatal and skin fibroblast cultures of infants with and without cleft palates with the hope that receptor levels can be shown to be a controlling factor in human cleft palate. If dilantin is given at an early stage in mice, it also produces cleft lip and cleft palate. We propose to include the study of dilantin induced cleft lip and palate in mice as a model of the fetal dilantin syndrome. Dilantin can form a reactive epoxide intermediate which may be related to its teratogenicity. The known differences in mixed function oxidase enzyme system in cleft palate susceptible and resistant strains of mice may account for the formation of this intermediate which may covalently bind to target tissues at a critical period. We would also like to delineate the enzymatic reactions involved in phenytoin metabolism and identify the contribution of the parent compound or its metabolite(s) to the teratogenic effect. In short, we hope to delineate the molecular chain of events involved in the action of a teratogenic drug in both animals and humans with cleft (lip) palate as a model of drug-induced craniofacial anomalies.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $131,370

6.0004, STUDY OF A VIRUS-INDUCED CRANIOFACIAL ANOMALY

H.W. Toolan, Inst. for Medical Research of Bennington, *110 Hospital Dr., Bennington, Vermont* 05201 (R01 DE 05541-01)

Hamsters infected in utero through injections of their mothers with the parvovirus H-1, develop craniofacial anomalies with predictable regularity. We propose, by means of immunofluorescent techniques as well as histological and electron microscopic studies, to trace this teratogenic virus from the time and site of maternal injection to the embryonic cells affected. We hope in this manner to determine crucial areas in the developing embryo involved in the induction of anomalies before any change in gross morphology can be observed; we may also be able to pinpoint regions of importance where anatomical aberrations per se are not seen. A large series of pregnant hamsters will be injected on each day of the gestation period of 16 days so that the effect of the virus infection on the developing embryo from the time of coitus to delivery can be assessed - in particular as such effects relate to the induction of craniofacial deformities.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

6.0005, STUDIES ON TERATOGENIC EFFECTS OF LOW LEVELS OF MERCURY AS FOUND IN DENTAL OFFICES

G.S. Rao, American Dental Assn., Health Foundation, Division of Biochemistry, *211 E. Chicago Ave., Chicago, Illinois* 60611

At least 10 percent of the dental offices in the U.S. are estimated to have atmospheric levels of mercury vapor in excess of the value of 0.05mg mercury/m3 set by the National Institute of Occupational Safety and Health. The objective of the proposed research project is to evaluate in Wistar rats the potential teratogenic effects of low levels of mercury vapor comparable to those found in typical dental offices, i.e., 0.02-0.20mg/m3. Two series of experiments will be conducted. Series I Experiments will be conducted according to the standard teratology protocol and involve continuous mercury vapor exposures, 24 hr/day during pregnancy. Series II Experiments will constitute a simulation of the exposure to mercury vapor reflecting the manner in which female personnel are exposed in the dental office, i.e., 8 hr/day prior to and during pregnancy. The effect of maternal mercury exposure on litter size, fetal death, resorption and the incidence of congenital malformations (craniofacial, skeletal and soft tissues) wili be determined. Also, the effect of mercury exposure on maternal and fetal weight gain as well as the effect of dose on the distribution of mercury in the tissues will be assessed. These studies are expected to provide a definitive answer to the question whether the exposure to low levels of mercury as found in dental offices is teratogenic to developing mammalian embryos.

SUPPORTED BY
American Fund for Dental Health $21,455

ETIOLOGY - GENETICS

6.0006, HETEROGENEITY IN OSTEOGENESIS IMPERFECTA

L.S. Levin, Johns Hopkins University, School of Medicine, Dept. of Otolaryngology/Medicine, *725 N. Wolfe St., Baltimore, Maryland* 21205 (R01 AM 25869-01)

The purpose of this study is to further delineate the genetic heterogeneity which has been shown to exist in osteogenesis imperfecta (O.I.), since a satisfactory classification has never been proposed. The proposal concentrates on detailed evaluation of portions of the phenotype never previously studied in detail: the dentition, hearing, and cardiovascular status. Probands ascertained from the files of the Moore Genetics Clinic as well as from local organizations of families with O.I. will be contacted and asked to participate. Histories, to include pedigree analysis, routine physical examination, otolaryngologic evaluation, dental examination (to include radiographs), echocardiogram and a full audiologic evaluation will be performed. Normally exfoliated and extracted teeth on patients with O.I. will be studied using the light and scanning electron microscopes to determine what differences exist between the teeth in the various forms of O.I. Genetic analysis will include the techniques of principal-components and cluster analysis to systematically identify subgroups. The study will provide accurate description of the phenotype of the various forms of O.I. prior to initiation of biochemical studies.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Arthritis
Metabolism & Digestive
Diseases $64,671

PATHOLOGY

6.0007, ORAL PATHOLOGY PROGRAM GRANT

R.J. Gorlin, University of Minnesota, Minneapolis Campus, School of Dentistry, Dept. of Oral Pathology, *6 Morrill Hall, Minneapolis, Minnesota* 55455 (R01 DE 01770-17)

Our research objectives and methods encompass: 1. Recognition, delineation, and analysis of new and recognized syndromes affecting the head and neck, especially those of facial dysmorphology and deafness. Study involves several parameters: a) clinical definition of new entities, b) cephalometric study, c) inheritance pattern (if not already known), d) dermatoglyphic analysis, e) biochemical investigation of autosomal recessive and X-linked disorders and f) some histochemical studies. 2. Epidemiologic studies of Amerindian and Inuit groups with regard to focal epithelial hyperplasia. 3. Chromosomal studies on karyotype clonal evolution of cancer cells and sister chromatid exchanges in a number of viral disorders and 'cancer syndromes'. 4. Studies of inborn errors of glycoconjugate metabolism.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $104,313

6.0008, CRANIOFACIAL ANOMALY SYNDROMES

M.M. Cohen, University of Washington, School of Dentistry, Dept. of Oral Surgery, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (R01 DE 04502-03)

The specific objectives of the proposed research are: (1) To analyze the relationship between facial anomalies and the spectrum of holoprosencephalic disorders and to elucidate the genetic factors behind this relationship, (2) To analyze the genetic factors operative in craniosynostosis and craniosynostosis syndromes, and to further delineate craniosynostosis syndromes, (3) To analyze the genetic factors operative in branchial arch syndromes and to further delineate branchial arch syndromes, and (4) To describe and analyze new genetic malformation syndromes and to further delineate incompletely documented syndromes.

The projects in this grant proposal focus on the delineation of craniofacial anomaly syndromes. Various methods appropriate to the specific studies listed are proposed, including clinical, genetic, anthropometric, and radiographic studies.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $63,953

6.0009, HISTOCHEMICAL STUDY OF THE HUMAN MASTICATORY MUSCLES

C. Vignon, Universite dAix Marseille, Faculte de Chirurgie Dentaire, Dept. of Biology & Fundamental Materials, *Charles Livon Blvd., Jardin Emile Duclaux, 13007 Marseille, France*

The application of histochemistry on muscular tissues enables us to establish the distribution of the different fiber types. Knowledge of the histo-enzymological profile of a muscle is essential in order to appreciate the secondary modifications, and these results are of great use in muscular pathology. Our first objective was to know the structure of the human masticatory muscles. This work has led us to specify the particular aspect of five groups of masticatory muscles with the adult and with the child. With individuals showing parafunctions or a defective occlusion, structural modifications seem to indicate that there exists a correlation between the morphology and the function of these muscles. We are looking for the role of a nervous factor in certain muscular attacks when there are no existing functional anomalies. Our present aim is to contribute to the study of facial muscular algesia.

SUPPORTED BY
Universite dAix Marseille funds n.a.

DIAGNOSIS & TREATMENT

6.0010, EVALUATION OF CRANIOFACIAL SURGERY - I. EVALUATION OF CRANIOFACIAL SURGERY PERFORMED BY PAUL TESSIER, M.D.

S. Pruzansky, University of Illinois, Medical Center at Chicago, Abraham Lincoln School of Medicine, Dept. of Pediatrics, *1853 W. Polk St., Box 6998, Chicago, Illinois* 60680 (P01 DE 02872-100038)

The Center is in a unique position to evaluate craniofacial surgery for three reasons: 1. It possesses the only longitudinal data base documenting the wide range of expression and malformations associated with the syndromes of Apert, Crouzon, hemifacial microsomia, mandibulofacial dysostosis, and the various median and paramedian cranio-orbito-facial deformities including orbital hypertelorism. This material has been subjected to continuous analysis resulting in a cadre of professionals well informed in the variant pathologies exhibited by these patients. 2. Probably the best documentation of patients operated by Paul Tessier which includes multiple procedures on 26 different patients. 3. An increasingly growing series of patients operated upon by Michael Schafer, M.D. who trained with Dr. Tessier in Paris and with Dr. Ian Munro in Toronto.

With these data in hand, we can evaluate the effects of surgery on facial growth and related functions affected by the surgery including, vision, eye motility, respiration, speech and masticatory function.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $33,998

6.0011, STUDIES IN MAXILLOFACIAL PROSTHETICS

H.O. Gold, University of Illinois, Medical Center at Chicago, Abraham Lincoln School of Medicine, *1853 W. Polk St., Box 6998, Chicago, Illinois* 60680 (P01 DE 02872-100053)

Evaluation of Multi-Abutment Fixed Prosthesis as an Alternative to Secondary Bone Grafting.

Except where secondary bone grafting (subsequent to primary lip repair) is required to reconstruct the nasal sill, the advantages for this operation can be met by fixed prostheses. These advantages include (1) permanent retention following orthodontic repositioning of palatal shelves; (2) replacement of missing dental units; (3) obturation of residual clefts in the alveolar region and hard palate; and (4) fixation of the 'floating' premaxilla, and (5) increased biting force of the premaxilla.

A preliminary report on the technology has recently been published by Gold and Pruzansky (Jour. Prosth. Dent. 1979). The cumulative experience in this clinic is allowing for long term evaluation in relation to the above factors as well as to maintenance of dental and periodontal health as well as patient satisfaction.

Evaluation of Vaginal Stents. Design and utility of vaginal stents employed in vaginal reconstruction. Surgeons and patients are being followed to evaluate the benefits of custom designed vaginal stents.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $26,402

6.0012, EXPERIMENTAL BASES FOR CRANIOFACIAL DYSJUNCTION

L.A. Whitaker, University of Pennsylvania, School of Medicine, Dept. of Surgery, *36th & Hamilton Walk, Philadelphia, Pennsylvania* 19174 (R01 DE 04110-03)

An experimental procedure is proposed to study the effects of extensive soft tissue dissection, craniofacial dysjunction, and bone grafts at osteotomy sites on the growing face of the Rhesus monkey. Data collected from such experimental procedures would provide an experimental basis for determining the amount of growth disturbances produced by extensive soft tissue dissection, release of all known sutural, bony, and synchondrosis attachments of the growing face to the skeleton, and the superimposed effect of bone grafting. Such data, by delineating the effect of extensive surgical procedures on the growing face of the Rhesus monkey, would provide an experimental basis for the timing of corrective surgical procedures for major craniofacial birth and traumatic defects in the human. This is a currently major unknown area in craniofacial surgery. It is indeed not known whether separation of the bony face from the skull has any effect either beneficial or detrimental on the growing face.

Surgical procedures duplicating those done in the human for craniofacial dysjunction, including extensive soft tissue subperiosteal dissection, osteotomies through suture attachments of the face to the skull and through the principal synchondroses and bony attachments of the face to the skull, and bone grafting, are proposed in the Rhesus monkey. By means of vital dyes, markers, serial standardized x-rays, dental study models, photographs, and clinical observations with precise measurements over a period of two and one half years in the Rhesus monkey, a standardized growth experience equal to about seven years in the human can be observed. Data accumulated in the monkey should give insight into what can be expected in the growing face of the human which has had such an operative procedure.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

6.0013, CRANIOFACIAL ANOMALIES - TREATMENT EVALUATION

J.P. Krischer, Tufts University, Boston Campus, School of Dental Medicine, Dept. of Oral Health Science, *136 Harrison Ave., Boston, Massachusetts* 02111 (R23 DE 04551-02)

This research is directed at the development and application of quantitative measures in treatment planning and evaluation in the management of craniofacial anomalies. Analytic techniques of decision theory, more specifically, multiattribute utility theory, will be the principal means for assessing preferences, priorities (relative importance of individual aspects of treatment outcomes) and group or team decision making dynamics. In addition to studies directed toward evaluation of outcomes, the research will also focus on the team decision making process and the dynamics through which team members interact and resolve individual differences in arriving at consensus. Models built on Pareto optimal or group Bayesian approaches will be developed and applied in actual treatment planning situations. Results during the current project year have yielded improved methods for utility function assessments facilitating application to clinical settings. Assessments and testing of results with actual case material is planned.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$32,491

6.0014, PALATAL LIFTS FOR TREATING PATIENTS WITH DYSARTHRIA

J. Aten, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Speech Pathology Section, *5901 E. 7th St., Long Beach, California* 90822 (600-001-P)

Data collection on subjects is completed with the current N of 16. The project is in the final stage of data analysis and rough drafting of a manuscript. The major contributions of the study appear to be in three areas: (1) Reporting major advances in the design of the palatal lift, particularly with edentulous patients who have had the lift attached to their maxillary dentures. The use of 20 gauge wire to extend the lift from the dentures provides flexibility to make minute adjustments in the A-P, Lateral and Superior dimensions. These adjustments based upon observations of the degree of velopharyngeal closure using cineradiography appear to result in a more effective utilization of the lift to reduce nasal emission and hypernasality while insuring a fitting that is best tolerated by the patients. (2) Combining the above with acoustic/perceptual judgments of intelligibility of speech pre-post fitting results in a more effective procedure than either approach or discipline working in isolation. (3) Speech intelligibility measures are quite variable between subjects. No general group statement can be made predicting the benefit any particular patient may receive from a palatal lift. We have observed high variability from patient to patient as he differentially responds to the procedure and subsequent rehabilitation strategies. For some patients the lift appears to have had a facilitating effect on velopharyngeal closure whereby the patient no longer needed to wear the lift as verified by increased velar movement and as judged by reduction in hypernasal emission. Some of the variability can be attributed to the subject sample which included numerous patients with multiple system involvement (i.e., respiratory, phonatory, and articulatory as well as resonatory). (4) The need to follow patients closely after the fitting and make 'comfort adjustments' as their tolerance of muscle movement potentials change appears to justify the more flexible (wire) extension approach. Another two months is anticipated for data analysis and final draft for typing.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

VII. MALOCCLUSION

ETIOLOGY - DEVELOPMENTAL BIOLOGY

7.0001, EXPLANTATION OF DENTAL LAMINA

W.A. Miller, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (R01 DE 02908-06)

It is proposed to study the development of the dental lamina by surgical transplantation of tooth germs and dental lamina in the Australian marsupial Trichosurus vulpecula. Radiographic and histological analyses will be performed.

The role of basement membrane and basal lamina in dental ontogeny will be investigated by various enzymatic separation techniques with subsequent heterologous recombinations cultured on the CAM. Cell culture studies on the role of various cell populations within the dental pulp during differentiation and repair will be continued.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

7.0002, PRENATAL ORIGINS OF POSTNATAL DENTOFACIAL VARIABILITY

A.R. Burdi, University of Michigan, Ann Arbor Campus, Medical School, Dept. of Anatomy, *1335 E. Catherine St., Ann Arbor, Michigan* 48104 (R01 DE 03443-07)

Purposes of this project include (1) exploration of the prenatal origins of human postnatal dentofacial growth patterns and polymorphisms; and (2) the design of histologic criteria which would be sensitive and reliable enough to demonstrate regular and variable patterns of growth changes according to the vital statistics and familial history of the abortuses studied. Aim one will be pursued using a 'developmental staging' scheme for dentition, facial primordia, craniofacial bones as seen in serial histologic sections of over 685 human abortuses representing the key time periods of craniofacial development. Intra- and inter-individual data will be reduced and analyzed on an information background of the abortus which includes sex, race, chromosome information (when practical), age and available histories of the pregnancy and family. Aim number two is intended to show the regular variations in age-typical growth stages. Data on tooth morphogenesis, organ and skeletal development, for example, will be handled using correlation matrices similar to those used for postnatal studies. These interorgan-inter-regional correlation matrices have the capacity to retrospectively explain, in part, why specific organs and/or system cluster in birth defect syndromes, e.g., orofaciodigital. Moreover, encoded background histories on the pregnancy and available karyotypes, for example, can help explain defects as either isolated or heritable events.

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SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

7.0003, TOOTH ERUPTION/MOVEMENT/RESORPTION - BIOCHEMICAL ASPECTS

Z. Davidovitch, University of Pennsylvania, School of Dental Medicine, Dept. of Orthodontics, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (R01 DE 03619-07)

The objectives of this work are to investigate the role of cyclic nucleotides (cAMP and cGMP) and prostaglandins (PGE2 and PGF 2 alpha) in the mechanism of alveolar bone and periodontal ligament remodeling during tooth eruption, resorption and movement; to study the effects of parathyroid hormone, calcitonin, imidazole and theophylline on cyclic nucleotide and prostaglandin levels in tissues surrounding erupting, resorbing and moving teeth. The tissue samples will be obtained from kittens and adult cats.

Prostaglandins have been extracted and measured in alveolar bone extracts following orthodontic treatment. Elevation in PGE2 levels were found at tension sites after 1 day of treatment, and at compression sites after 7 days. Work is in progress on the development of a method for the immunohistochemical localization of PG's in jaw sections, as is presently done for cyclic nucleotides in our laboratory. Preliminary effort will attempt to localize PC's by transmission electron microscopy, as performed for cyclic nucleotides.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$122,549

7.0004, ELECTRON MICROSCOPIC CYTOCHEMISTRY OF THE STRESSED PERIODONTAL LIGAMENT

E.A. Diaz, University of Puerto Rico, Medical Sciences Campus, School of Dentistry, Dept. of Orthodontics, *Rio Piedras, Puerto Rico* 00931 (R23 DE 05548-01)

The purpose of this research project is to elucidate the interrelationship that exists between fibroblast and collagen in the periodontal ligament (P.D.L.) during tooth movement.

To achieve this purpose the acid and alkaline phosphatase EM cytochemical techniques of Barka and Anderson (1962), and Yoshiki and Kurahashi (1971-72) will be utilized to evaluate lysosomal function and collagen phagocytosis in fibroblast of the orthodontically-stimulated rodent P.D.L. Maxillary right first and second molar periodontal ligaments of 30 day old Holtzman rats will be subjected to an initial orthodontic force of 20 grams for 3/4, 6 hours, 4 and 8 days.

Along with their controls these ligaments will be individually incubated, stained and processed for electron microscopy. The fibroblast close to bone, middle and cemental areas of the P.D.L. will be studied in both the pressure and tension sides to determine relationships between lysosome and the so called 'collagen containing profiles'. The different time intervals in which the ligament cells will be studied should provide ultrastructural data on fibroblastic behavior during the initial middle and late reparative stages of tooth movement.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$25,755

7.0005, CHEMISTRY AND BIOSYNTHESIS OF CONNECTIVE TISSUE

G.R. Martin, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Connective Tissue Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00009-18 DB)

The purpose of this project is to study the formation, function and destruction of connective tissue components in normal and diseased states. Particular attention is directed toward collagen and proteoglycan. Current aspects of the project include (1) characterization of the matrix components in a tumor which produces basement membrane, (2) the role of collagen in diseases, and (3) interaction of tumor cells with collagens.

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SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$109,942

ETIOLOGY - GENETICS

7.0006, CRANIOFACIAL VARIATION AND MALOCCLUSION IN FAMILIES

J.E. Harris, University of Michigan, Ann Arbor Campus, School of Dentistry, Dept. of Orthodontics, *Ann Arbor, Michigan* 48104 (R01 DE 03013-11)

It is the purpose of this investigation to determine the extent of applicability of the polygenic model of inheritance to the analysis of malocclusion. Put into operational terms, this study is designed to determine whether different morphologic components of the skull are under equal polygenic control and whether these morphologic elements exhibit genotypic independence.

Previous investigation of family data has supported the contention that craniofacial variation generally, and Class II div. 1 specifically, represent polygenic inheritance. The application and importance of these findings to diagnosis and treatment planning for the orthodontic patient has been demonstrated by the previous research supported by this grant. Further refinement of knowledge of the detailed inheritance in the craniofacial complex depends upon the utilization of an idealized study population.

The Nubian population of Ballana, Egypt is uniquely suitable for the rigorous evaluation of the polygenic model of inheritance. The Nubian family data comprises a uniquely homogenous population of known origins, established family pedigrees, multiple marriages, first cousin marriage patterns, and stable culture and diet. The cephalometric, cast, dental record, and anthropometric data have already been collected and are housed in the Department of Orthodontics, School of Dentistry University of Michigan.

Multivariate techniques of analysis will be used to assess the role of heredity in the development of the craniofacial complex.

BIBLIOGRAPHIC REFERENCES: A skull with silver bridge to replace central incisor: Iskander, Zaky and Harris, James E. Anneles Du Service Des Antiquites De L' Egypte Tome LXII - (1977).

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

7.0007, GROWTH AND DEVELOPMENT OF THE ODONTOSTOMATOGNATHIC SYSTEM IN TWIN CHILDREN

G.H. Sperber, University of Alberta, School of Dentistry, Dept. of Oral Biology, *Edmonton, Alberta, Canada* T6G 2N8

An examination of the jaws and teeth of growing twin children in order to establish the frequency of dental malocclusion and deviations of jaw formation within twin pairs. From the data collected, the dental and orthodontic treatment needs among the population sampled can be related to the manpower supply available to provide the required treatment. Data collected on growth phenomena of the jaws and teeth between identical and non-identical twins will lead to a greater understanding of the relative roles of genetic and environmental factors in determining the ultimate shaping and functioning of the jaws, teeth and face.

SUPPORTED BY
Canadian Dept. of National
Health & Welfare funds n.a.

ETIOLOGY - FUNCTIONAL EFFECTS ON MORPHOLOGY

7.0008, EFFECT ON CORONOID PROCESS OF TEMPORALIS MUSCLE REMOVAL (RABBITS)

N.N. Soni, Howard University, Graduate School, *2400 6th St. N.W., Washington, District of Columbia* 20001 (S06 RR 08016-090019)

This project is part of a broader program (RR 08016-09) whose summary states: A renewal application is made for continued minority biomedical support for the Biomedical Interdisciplinary Project at Howard University. It consists of individual research elements with biomedical relevance and requests for support of strong undergraduate and graduate student research participation. The subject areas of Botany, Chemistry, Dentistry, Immunology, Psychology and Zoology are represented among 19 research project elements organized by individual faculty members or collaboratively among faculty in two or more disciplines.

Support is requested for visiting scientists to serve as a part of a Seminar-Science Conference component designed to promote University-wide communication among faculty and student scientists at Howard.

Overall, a program is proposed which will ultimately increase the biomedical research potential at Howard and add to the pool of minorities trained and prepared to perform at a high level in biomedical research.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health, Div. of
Research Resources funds n.a.

7.0009, EXPERIMENTAL STUDY ON THE ETIOLOGY OF MALOCCLUSION

E.P. Harvold, University of California, San Francisco Campus, School of Dentistry, Center for Craniofacial Anomalies, *551 Parnassus Ave., San Francisco, California* 94122 (R01 DE 02739-10)

This proposal is based on the premise that malformation of cranioskeletal structures during growth is influenced by alterations in muscle activity affecting bone remodeling and skeletal structure. It is suggested that modification of sensory input affecting reflexive pathways of the central nervous system alters this muscular activity. This investigation attempts to define some of the on-going changes in craniofacial muscle activity during development of predictable morphologic alterations in three experimental models utilizing rhesus monkeys. Paired animals in each model will receive intramuscular and surface electrodes in three muscles selected as representative of change in tone and activity. Analysis of EMG data is carried out by computer programs designed to compare results of one muscle under four conditions: 1) at resting level, 2) during increased load on the mandible, 3) during elicitation of the jaw opening reflex, and 4) in masticatory movements. The trend in intensity of EMG frequency of units in EMG, and discharge patterning of single motor units will be analyzed over successive recording sessions during the development of the morphologic alterations.

At this point in time the work is concentrated on the experimental model for the study on oral respiration. A series of muscles, specially recruited for oral respiration, have been identified. The sequence of recruitment and the concomitant morphologic changes which result in dental malocclusion are being studied.

BIBLIOGRAPHIC REFERENCES: Harvold, E.P. and B. Tomer. Primate experiments on jaw and dental arch morphogenesis. Amer. J. Orthod. 1978. Miller, A.J., Electromyography of craniofacial musculature during oral respiration in the rhesus monkey (Macaca mulatta). Arches. Oral biol., 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

7.0010, EXTENSIBILITY CHARACTERISTICS OF HUMAN CHEEK

S. Weinstein, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Orthodontics, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 04047-03)

The force-displacement characteristics of the cheek will be studied to: a) Evaluate the forces generated by the displaced cheek by the impingement of certain orthodontic appliances, b) Measure the 'rest-displacement' of the cheek associated with the equilibrium position of the natural dentition. A hydraulic system using a slave and master electroformed bellows with LVDT devices to monitor both force and displacement will be activated by an analog controller. Using computer programs for data taking, calibration, and analysis, data on two groups of subjects will be taken: 1. An adult population for the orthodontic appliance impingement study, and 2. An adult population destined to receive immediate full dentures.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$70,181

7.0011, STRAIN IN THE FACIAL BONES

W.L. Hylander, Duke University, School of Medicine, Dept. of Anatomy, *Box 3711, Durham, North Carolina* 27710 (R01 DE 04531-03)

The research proposed here is designed to contribute to an understanding of the function of the primate craniofacial region. Functionally the primate craniofacial region is dominated by the masticatory apparatus. This research will analyze how masticatory forces are dissipated throughout the primate face. This in vivo analysis of strain in the facial bones of Macaca fascicularis will be accomplished using strain gauges. Rather than using single-element strain gauges, rosettes (three strain gauge elements with a known orientation to one another) will be bonded directly to facial bones with methyl-3-cyanoacrylate. The restrained macaque will then bite a transducer or chew various types of foods and bone strain will be recorded on a multichannel chart recorder. In order to precisely correlate the animal's behavior with patterns of bone strain, the animal and the chart recorder will be videotaped. With a special effects generator, a split screen display of both animal and recorder will be produced and recorded.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$21,962

7.0012, LONG-TERM EFFECTS OF HEAVY FORCE ON THE MAXILLA

T.M. Graber, University of Chicago, School of Medicine, Dept. of Pediatrics, *5801 S. Ellis Ave., Chicago, Illinois* 60637 (R01 DE 04599-01)

The objective of the project is to study the effects of intermittent retractive and protractive heavy ('orthopedic') forces on the maxilla in the growing Saimiri sciureus. Special emphasis will be placed on the long-term effects after discontinuation of force application. The longitudinal influence of force application on the craniofacial morphology will be examined with roentgenographic cephalometry, using metallic implants and in vivo bone markers.

The sample consists of twelve growing male squirrel monkeys of known chronological age. The monkeys are divided into three groups, two experimental, and one control; with four monkeys in each group. The monkeys in one experimental group are subjected to a retractive force, and the monkeys in the other experimental group are subjected to a protractive force. Starting when the animals were approximately 12 months of age, the traction will be applied for a period of 6 months (treatment period). Using cemented gold splints on the maxillary teeth and restraining collars for force attachments, a force of approximately 75 grams is being applied intermittently for about 14 hours/24-hour period. The control monkeys have gold splints and restraining collars but no traction. Tantalum implants, oxytetracycline and Procion dyes are used as identification markers in all animals. Lateral cephalometric radiograms will be taken during force application and a 12-month post-treatment observation period. At the end of the observation period, all animals will be sacrificed. The results will be based on histological examination, serial superimposition of cephalometric tracings and cephalometric linear and angular measurements, and dry skull morphology.

This research is currently in progress. The application is submitted in order to solicit financial support for the time period involving the last part of the posttreatment observation period and a subsequent period for preparation, analysis and interpretation of data.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

7.0013, IN VIVO EXPERIMENTS ON BONE MUSCLE INTERACTION

G.J. Chierici, University of California, San Francisco Campus, School of Dentistry, Dept. of Growth & Development, *551 Parnassus Ave., San Francisco, California* 94122 (R01 DE 05119-02)

Our experimental clinical investigations suggest that new bone formation will extend bone perimeters when adjacent connective tissue is subjected to tension and functional forces are transmitted beyond the bone margins. This proposal is based on the concept that neuromuscular activity produces biophysical stimuli and that these stimuli influence the differentiation of cells and results in bone formation. The experimental model is the rhesus monkey in which symmetric forces acting on the parietal bones are caused to become asymmetric by detachment of the right temporal muscle. The investigation will examine the effects of this functional imbalance in 1) bone margins, 2) morphology of the sagittal suture, 3) the normal and detached muscle, and 4) the skeletal and muscle function. The effects on level and pattern of muscle activity will be studied by EMG and histologic methods will be employed for examination of the morphologic findings.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $41,596

ETIOLOGY - CRANIOFACIAL GROWTH

7.0014, NUBIAN GROWTH, DEVELOPMENT, AND ORAL HEALTH

J.E. Harris, National Bank of Egypt, *Cairo, Egypt* (03-011-N)

SCOPE: To investigate the etiology of malocclusion by studying the craniofacial growth, dental development, and oral health in a racial isolate, i.e. the Nubian Egyptian. The modern Nubians (Ballana), together with their remains, provide a relatively homogeneous population base extending back to 200 A.D. Here the opportunity to closely inspect the interaction of heredity and environment on dental disease, especially malocclusion, is optimal.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
Fogarty International Center funds n.a.

7.0015, THE NATURAL HISTORY OF CLEFT LIP AND PALATE - TYPE AND FREQUENCY OF MALOCCLUSION IN CLEFTS (CL/P)

H. Aduss, University of Illinois, Medical Center at Chicago, Abraham Lincoln School of Medicine, *1853 W. Polk St., Box 6998, Chicago, Illinois* 60680 (P01 DE 02872-100036)

For summary: see 5.0006.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $4,521

7.0016, THE NATURAL HISTORY OF CLEFT LIP AND PALATE - III, A QUANTITATIVE ANALYSIS OF THE MAXILLARY ARCH IN CL/P

H. Aduss, University of Illinois, Medical Center at Chicago, Abraham Lincoln School of Medicine, Dept. of Pediatrics, *1853 W. Polk St., Box 6998, Chicago, Illinois* 60680 (P01 DE 02872-100037)

For summary: see 5.0007.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $4,521

7.0017, FACIAL AND DENTAL GROWTH IN PRE- AND POST-ADOLESCENTS

C.F. Moorrees, Forsyth Dental Center, *140 Fenway St., Boston, Massachusetts* 02115 (R01 DE 02873-12)

Twins, their age-matched siblings and parents are studied longitudinally to obtain an accurate estimate of facial, dental and somatic growth, including their interrelationships, with reference to adolescent growth rates and patterns, physique, physiologic and chronologic age scales.

Individual differences in growth rate, size and timing of development will be examined, together with an assessment of the short-term predictability of facial growth trends and an analysis of within twin pair differences according to sex and zygosity.

The main twin sample consists of 414 twin pairs, averaging 9 years of follow-up, with 160 male pairs, 134 female pairs, and 120 male-female pairs. On the basis of blood typing analyses, 94 male pairs and 88 female pairs were classified as monozygotic twins. More than 400 siblings of the twins have also participated in this longitudinal study.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$232,578

7.0018, ERUPTION RATES OF RATS' MAXILLARY INCISORS UNDER INTRUSIVE FORCES

R.A. Burn Murdoch, University of London, University College Hospital Medical School, Dept. of Physiology, *University St., London WC1E 6JJ, England, United Kingdom*

Various mechanisms have been put forward as possible causes of tooth eruption. Previous studies have tried to test these hypotheses by measuring rates of eruption. As rates could be affected by variations in not only the force acting on the tooth, but also in the resistance exerted by the periodontal membrane to that movement, it was decided to try to measure these forces.

In two previous studies intrusive forces were applied to rat and rabbit incisors and the eruption followed by recording the position of marks on their labial surfaces at intervals of 12 or 24 hours. It is possible that applying intrusive forces for this length of time could alter the process of eruption. Also, neither study reported the relationship between the magnitude of the applied force and the rate of eruption under it, from which something about the resistance that the periodontal membrane exerts could have been learned.

Therefore it was decided to measure the eruption rates of rats' incisors under intrusive forces using a device that would continuously monitor the movements of the teeth.

A suitable technique has now been developed.

SUPPORTED BY

(No Supporting Organization Reported)	funds n.a.

PATHOLOGY - CRANIOFACIAL GROWTH

7.0019, GROWTH AND DEVELOPMENT OF THE HUMAN HEAD

E.R. Richardson, Meharry Medical College, School of Dentistry, Dept. of Orthodontics, *1005 18th Ave. N., Nashville, Tennessee* 37208 (R01 DE 02862-14)

During the next year, this research team plans to critically analyze the facial profile of the various ethnic groups. Hopefully, this information will be helpful to scientists and clinicians in their endeavors to understand the physiogomy of the human face. It may also contribute to the clinicians' efforts to make orthodontic care more readily available to all persons regardless of ethnic background. Additionally, the team will attempt to assess the effects of factors other than pressure habits on the occlusal positions of the secondary dentition.

BIBLIOGRAPHIC REFERENCES: Richardson, E.R. (1978) Effects of Nutrition on the Development of Teeth and Dental Caries: A Review. The Quartery of the National Dental Association. 36:81-88. Khurana, H.S. and Malhotra S.K. (1978) Dental Emergencies chapter in book Immediate Care of the Sick and Injured Children. Edited by Shiv K. Dube and Sophie H. Pierog. The C.V. Mosby Company, St. Louis, pp. 172-179.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$151,157

7.0020, PREDICTION OF TOOTH DISPLACEMENT

C.J. Burstone, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Orthodontics, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 03545-07)

The aim of this research is to accurately predict three-dimensional displacements of teeth for any applied force system, to quantify these results in terms of centers of rotation, and to estimate stress-strain characteristics at the tooth-periodontal ligament and periodontal ligament-alveolar bone interfaces.

The translations and rotations of teeth will be determined using non-invasive, state-of-the-art techniques of hologram interferometry.

The experimental data will also be used to develop a mathematical model for prediction of stress-strain characteristics of the periodontal ligament; this model will by synthesized using the finite element technique. The synthesis technique which will be developed herein will be a considerable improvement over present analytical techniques.

Stresses in the primate periodontal ligament will be estimated and related to one remodeling studied histologically.

Primary displacements (before any biologic changes such as bone apposition and bone resportion take place) of skull bones will be studied and related to secondary displacements (when biologic changes are present) using hologram interferometry.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$114,030

PATHOLOGY - PHYSIOLOGY

7.0021, QUANTITATION OF JAW FUNCTION

F.W. Worms, University of Minnesota, Minneapolis Campus, School of Engineering, Dept. of Mech Engin, *105 Morrill Hall, Minneapolis, Minnesota* 55455 (R01 DE 03528-06)

The overall objective or long term goal of the proposed research is the accumulation of quantitated data describing the human chewing function in terms of frequency, duration and amplitude. These parameters and their existing variations must be established in 'acceptable' or 'normal' or 'good' occlusions as best as these parameters can be morphologically defined in terms of dentition and skeletal pattern. Secondly, individual variation from time point to time point must be established for the same group. Thirdly changes associated with development must be established if growing dynamic states are to be investigated. Finally, given the above information the function of so called 'abnormal' or 'unacceptable' or 'malocclusions' can be quantitated and compared.

A stereo-photography system is being developed based on the use of a high-speed camera, whose view of a patient is split by prisms and mirrors to obtain stereo vision on each frame of film. LED are attached to lightweight frames located on the upper and lower jaw and show up as light spots on the film. A unique digitizing system is being devised to accelerate the data processing which includes three-dimensional matrix manipulation of data via a computer. Relative motion between the patients' jaws is displayed on a computer graphics screen.

BIBLIOGRAPHIC REFERENCES: Mechanics, Growth and Class II Corrections (with B. Hultgren, R. Isaacson, A. Erdman and F. Worms), Am. J. Orthodont. 74(4): 388-395, October 1978. Kinematics of Jaw Growth (with R. Isaacson, A. Erdman, B. Hultgren) J. Biomechanical Engineering, 100:May 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$106,294

7.0022, FUNCTIONAL PROPERTIES OF RABBIT JAW MUSCLES

Z.F. Muhl, University of Illinois, Medical Center at Chicago, School of Dentistry, Dept. of Orthodontics, *1853 W. Polk St., Chicago, Illinois* 60680 (R01 DE 04164-04)

The proposed studies will use the digastric muscle of the rabbit, simple model of an oral striated muscle, to develop an isometric length-tension sarcomere diagram. The digastric muscle tendon can be attached directly to an apparatus for measuring and recording active and passive muscle tension and muscle length. Sarcomere lengths will be measured from the digastric muscle, fixed at the end of the length-tension experiment by arterial perfusion of 10% formalin. Muscle fiber length and cross-sectional area will also be measured for use in constructing the isometric length-tension sarcomere diagram. The completed isometric length-tension sarcomere diagram will then be used to estimate force production capability of the intact digastric muscle. Additional animals will be sacrificed by fixing the head with the jaws in various functional positions. Muscle length and sarcomere length will be measured at these known jaw positions and compared to the independently determined values for muscle length and force production of the length-tension sarcomere diagram. These experiments should yield information about the range of muscle lengths and sarcomere lengths for the functional jaw positions and should also provide a good estimate of muscle force capability throughout the functional range.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $18,319

7.0023, INVESTIGATION OF TOOTH FORCES AND TOOTH MOBILITY

C.H. Gibbs, State University System of Florida, University of Florida, School of Dentistry, Dept. of Basic Dental Sciences, *Gainesville, Florida* 32601 (R01 DE 04350-04)

The basic nature of the force, duration and frequency of tooth contacts during bruxing and mastication will be investigated. The changes in nocturnal bruxing habits with modification in occlusion will be measured. Time dependencies among jaw movement, EMG activity and tooth force will be documented. Forces recorded during bruxism will be compared with forces recorded during chewing to evaluate the potential damage to the periodontium of bruxism in relation to mastication.

A system for measuring the jaw force has been developed as the first part of this project. This system deduces jaw force from variations in amplitude of introduced vibrations which are transmitted by the facial bones, periodontium, teeth and muscles. This system avoids using mouth appliances which could interfere with the preconscious jaw functions of chewing and bruxing. This vibration transmission system will be evaluated for use in measuring tooth mobility. The system appears useful in measuring muscle tension in limb muscles as well as jaw muscles.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $22,775

7.0024, MUSCLE ACTIVITY AND CONTROL IN MASTICATION

C. Gans, University of Michigan, Ann Arbor Campus, School of Literature Science & the Arts, Dept. of Biological Science, *Ann Arbor, Michigan* 48104 (R01 DE 05112-01)

Te masticatory reduction of food is a key preliminary to effective nutrient extraction, and the time and energy invested in chewing have been shown to vary with food type, consistency, and size as well as dentitional pattern. Food reduction involves more than simple linear or planar mandibular rotation (about the condyle); propalineal and transverse shifts are common, and mandibles move in a complex three-dimensional path. Food is reduced by being passed unidirectionally across the triturating surface when the teeth are nearest occlusion; during the rest of the mastication cycle, movements of tongue, lips, and the whole head return the bolus to the starting side of the active tooth row.

The forces required to maintain the mandible in its path consequently vary. Control of the cycle involves matching muscular activity to the demands at different parts of the orbit, reflecting in part the position, size and consistency of the food.

It is proposed to correlate movements and motor sequences in three mammals and three reptiles (possibly similar to precursors of early states of mammalian mastication), using wild (non-domesticated) animals, which have been conditioned to feed normally. Analysis will involve motion recording by cinematography, cinefluoroscopy, and strain gauge recording; the fiber types of the muscle will be characterized by histochemical assay, and fiber lengths and architecture determined, and their function during mastication noted by electromyography. From these data we hope to match muscle physiology and activity to the energy shifts of the moving system and to determine those aspects that seem to be maximized, and presumably most significant to the organism.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $59,011

7.0025, STUDIES ON STRESS-RELATED BONE RESORPTION

G.R. King, State University System of Florida, University of Florida, School of Dentistry, Dept. of Orthodontics, *Gainesville, Florida* 32601 (R23 DE 04844-02)

These experiments propose to deal specifically with the question of chemical mediation in one resorption stimulated by the application of force. Pilot data have supported the hypothesis that chemical factors in the local microenvironment of bones exposed to forces can stimulate increased release of calcium from fetal bones. It will be determined if this stimulation calcium release is also reflected by an increase in osteoclast numbers. If this correlation can be made, calcium release will be used as a bioassay for bone resorption in further studies of this phenomenon. Other major objectives will include a description of the effect of duration and degree of force application on the stimulation of such bone resorption mediator(s). Preliminary investigations will also be made into the chemical nature of this/these mediators(s). Correlations between the degree of root resorption in the test animals and amount of calcium release in the bioassay will also be made.

Using simple orthodontic appliances on rats, tipping forces of known magnitude will be applied. The tissue immediately surrounding the point of pressure application and similar areas from control animals will be excised, homogenized and cleared of cellular debris. After normalizing these homogenates for wet weight of sample, their ability to stimulate resorptive activity will be assessed by bioassay. The bone resorption bioassay to be used is based on the release of pre-incorporated 45Ca from the fetal long bones into a tissue culture medium which has been treated with a test homogenate.

The specific objectives will be carried out by generating and testing homogenates from alveolar bone exposed to forces for differing periods of time and of differing magnitudes. The chemical nature of this/these bone resorption mediator(s) will be investigated by perturbing the test homogenates and assessing alterations in their activities using the bioassay. The degree of root resorption will be assessed by quantitative SEM procedures.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $19,919

7.0026, SENSORY CONTROL OF OCCLUSION - MODEL SYSTEMS APPROACH

D.M. Senseman, Monell Chemical Senses Center, *3500 Market St., Philadelphia, Pennsylvania* 19104 (R23 DE 05536-01)

Recent experiments have focused on the chemical sensitivities of the oral cavity in the pulmonate snail Helisoma trivolvis to acceptable and non-acceptable taste solutions. It has been found that taste solutions prepared from acceptable food sources (i.e., wheat germ, fish meal) trigger the generation of the feeding motorprogram whereas non-acceptable taste solutions (i.e., 0.01 N HCl) inhibits the expression of this neural correlate of the consummatory feeding response. Control experiments have ruled out the possibility that the effect of acceptable solutions is directly on the central neurons as a result of leakage into the saline bathing the ganglia.

This work demonstrates that the snail's oral cavity contains sensory cells that are responsive to acceptable and non-acceptable taste solutions. Furthermore, information generated by these receptors is processed by the buccal ganglia to produce an adaptive response (i.e., feeding or the inhibition of feeding). Current efforts are directed toward identifying the synaptic inputs responsible for the excitation evoked by acceptable solutions and the inhibition evoked by non-acceptable solutions within this relatively discrete neuronal system.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $22,496

7.0027, THE EFFECTS OF INCREASED VERTICAL DIMENSION OF OCCLUSION

J.R. Blankenship, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *2215 Fuller Rd., Ann Arbor, Michigan* 48105 (506-001-F)

The effects of increased vertical dimension of occlusion on the masticatory system: The following hypotheses were tested: (1) Increased vertical dimension will not alter the functional morphology of the temporomandibular joints. (2) The posterior teeth with the bite raising appliances and teeth opposing these appliances were intruded relative to the alveolar process. There will be no change in the level of connective tissue attachment related to the cementum enamel junction of these teeth.

Significance of the research: (1) Bite raising appliances (a) are used often in restorative dentistry and in orthodontics. Various temporomandibular joint dysfunction syndrome. Both the short term and long term effects of such procedures are highly controversial. The proposed study would for the first time provide direct histometric and radioautographic evidence from controlled procedures of bite raising.

This study continues to be prepared for publication. Submission for publication is expected this year.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

7.0028, A STUDY OF THE CAUSE OF APPROXIMAL DRIFT OF TEETH

D.C. Picton, University of London, University College Hospital Medical School, Dept. of Experimental Dentistry, *University St., London WC1E 6JJ, England, United Kingdom*

CURRENT OBJECTIVE: To identify factors affecting the rate of approximal drift: (a) presence of opposing cusps; (b) cross-sectional area of the transeptal fiber bundles; (c) the importance of mobility of teeth relative to their neighbors.

APPROACH: Each factor is tested on a group of adult monkeys using the buccal segments as the experimental model.

PROGRESS: The presence of cusps appears to retard approximal drift significantly.

SUPPORTED BY

(No Supporting Organization Reported)	funds n.a.

7.0029, GNATHOLOGICAL INVESTIGATIONS IN DECIDUOUS DENTITIONS

M. Richter, Leopold Franzens Universitat Innsbruck, Dental Clinic, *Anichstr. 35, A6020 Innsbruck, Austria*

100 children with complete deciduous dentitions are studied. Emphasis is laid on the relation between interdigitation and the condition of the temporomandibular joint. Semiadjustable articulators and gnathological measures are used.

SUPPORTED BY

Leopold Franzens Universitat Innsbruck	funds n.a.

PATHOLOGY - SPEECH

7.0030, SPEECH AND HEARING TESTING AND RESEARCH UNIT

S.J. Peterson Falzone, University of Illinois, Medical Center at Chicago, Abraham Lincoln School of Medicine, Dept. of Otolaryngology, *1853 W. Polk St., Box 6998, Chicago, Illinois* 60680 (P01 DE 02872-100057)

For summary: see 5.0042.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$36,602

7.0031, CLEFT PALATE MALOCCLUSION AND LINGUAL ARTICULATION

D.W. Warren, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Dental Ecology, *Chapel Hill, North Carolina* 27514 (R01 DE 04267-04)

For summary: see 5.0044.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$44,110

7.0032, SPEECH ADAPTATIONS TO ORTHOGNATHIC SURGERY

P.S. Vig, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Orthodontics, *Chapel Hill, North Carolina* 27514 (R01 DE 05203-01)

The combined approach to dentofacial deformity using orthodontics and surgery can produce dramatic changes in morphology. Increasing numbers of patients are being treated in this way throughout the United States. Successful post-surgical physiologic adaptation in most patients permits unimpeded speech. However, speech patterns alter somewhat for most patients and some patients fail to make adequate compensatory adaptations for normal speech. In the absence of quantifiable data on form-function interrelations, individual response will continue to be unpredictable. Our preliminary studies on the effects of oral cavity size reduction on formant patterns suggest qualitative and quantitative associations between the nature of adaptive response and the size and geometric relationships between intermaxillary space and tongue. Rapid and dramatic response follows even small changes in oral volume.

This study will relate the morphologic changes which result from variety of surgical approaches to the patients' speech response. Hypotheses concerning structural change, stability and adaptation will be tested and data obtained which could render existing techniques of speech analysis as useful adjuncts to routine clinical diagnosis and treatment planning for orthognathic surgery.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$28,828

DIAGNOSIS & TREATMENT - ORTHODONTIC TREATMENT

7.0033, LONG-TERM EFFECTS OF ORTHODONTIC TREATMENT

C. Sadowsky, University of Illinois, Medical Center at Chicago, School of Dentistry, Dept. of Orthodontics, *1853 W. Polk St., Chicago, Illinois* 60680 (N01DE72401 (CONTRACT))

Evaluate the long-term effects of orthodontic treatment on the periodontal tissues, occlusal function, and tempo-mandibular joint. Also, attempt to identify factors related to the original malocclusion, treatment rendered, and post-treatment stability which may have an adverse effect on long-term effects and health.

SUPPORTED BY
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $0

7.0034, METHODOLOGIES TO MEASURE SOCIAL & PSYCHOLOGICAL FACTORS

J.E. Albino, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Behavioral Sciences, *3435 Main St., Buffalo, New York* 14214 (N01DE72499 (CONTRACT))

Develop new and meaningful methods for objective and standardized determination of the impact of malocclusion and its treatment. This first phase is specifically to determine whether it is feasible to develop a behavioral and dental instrument that will measure the impact of malocclusion on the individual. Such an instrument is to be pretested on a population of one hundred families with eighth or ninth graders not undergoing or planning orthodontic treatment and fifty families with children who are planning orthodontic treatment. A revised instrument will then be field-tested on another similar population of 150 families.

SUPPORTED BY
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $144,243

7.0035, LONG-TERM EFFECT OF ORTHODONTIC TREATMENT

A.M. Polson, Eastman Dental Center, *800 Main St. E., Rochester, New York* 14603 (N01DE82413 (CONTRACT))

The Contractor will design and conduct a two year study to evaluate the condition of the teeth, supporting structures (gums and bone), and occlusion (bite) of those who have had orthodontic treatment and to compare them with those who have not had orthodontic treatment. A study population of 100 or more patients who have completed full orthodontic treatment more than 10 years ago will be assembled. A suitable control group will also be obtained. The periodontal and general oral health and functional status of the study and control groups will be evaluated using various clinical examinations and measurements and radiographic techniques.

SUPPORTED BY
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $0

7.0036, LOW-FRICTION/ABRASION RESISTANT COATINGS FOR DENTAL AND MEDICAL APPLICATIONS

R.P. Kusy, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Orthodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130119)

The feasibility of utilizing commercially available low-friction/abrasion-resistant composite coatings for use in dental and medical appliances is being explored. From standards proposed by ASTM, the toxicological response of tissue to these coatings will be evaluated in two species, rats and rabbits. Applicability of the coatings in orthodontic appliances to reduce friction (facilitating tooth motion) and to the total hip prostheses to reduce wear debris will be evaluated both by laboratory (friction and wear) and clinical tests.

SUPPORTED BY
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $5,030

7.0037, CLINICAL EVALUATION OF THE ANDRESEN ACTIVATOR

E.P. Harvold, University of California, San Francisco Campus, School of Dentistry, Dept. of Orofacial Anomalies, *551 Parnassus Ave., San Francisco, California* 94122 (R01 DE 03503-08A1)

At the onset this proposal was based on the premise that the distribution of stress and forces on the jaws and teeth from the musculature at rest and in function have a significant impact on morphogenesis. It is suggested that a redirection of the force distribution to selected teeth and areas of the jaws will affect morphogenesis and can be utilized to prevent and correct dental malocclusions. One hundred and twenty children, all with a specific type of dental malocclusion, were included in the study. Sixty of the children were observed for two years before treatment was initiated. This group serves as control for the children who began treatment at the onset. After the two years of observation the control group was treated. All 120 children received the same type of treatment for two years in order to determine the general response to this therapy. After that the therapy was individualized. A series of theorems was formulated with regard to the response to the treatment and each theorem will be tested by selected measurements on cephalometric x-rays and casts of the dentition. Cephalometric x-rays in four projections and dental casts have been taken every six months together with clinical data.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

7.0038, DENTOFACIAL EFFECTS OF FORCES TO RETRACT THE MAXILLA

S. Baumrind, University of California, San Francisco Campus, School of Dentistry, Dept. of Orthodontics, *551 Parnassus Ave., San Francisco, California* 94122 (R01 DE 03598-05)

This project has two areas of concern: The first is the quantitative measurement of changes in the conformation of the skull and jaws (bone remodeling), and of alteration in the thickness and contour of the pharyngeal and facial soft tissues associated with certain types of orthodontic treatment. The design of the study is empirical and naturalistic. Independent samples of treated cases are selected retrospectively from the clinical practices of expert clinicians, each of whom has employed the extraoral or intra-oral treatment technique of his choice to restrain the forward development of the maxilla.

The second area is the development of special computer-aided methods for use in craniofacial research. These methods include techniques for rapid and precise data reduction from lateral skull radiograms and for the efficient conduct of hypothesis testing experiments upon large merged data bases of stored craniofacial measurements of different types.

The methods and technology developed in the second area will be used in the analysis of the data acquired in the first area.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

7.0039, FORCE SYSTEMS FROM ORTHODONTIC APPLIANCE

C.J. Burstone, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Orthodontics, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 03953-05)

The study is designed: 1) to determine the force systems delivered from orthodontic appliances and configurations; 2) to develop a mathematical model which has the capacity of predicting orthodontic force systems; and 3) to develop computer techniques that can optimize appliance design.

Force systems will be determined by two methods: 1) the analytical, and 2) the experimental. The analytical technique is based on beam theory that is capable of handling large deflections in three dimensions. The experimental component of the project will use a specially designed 1) force transducer to measure forces and moments in three dimensions; 2) and a stereometric system to accurately determine wire-attachment geometry.

BIBLIOGRAPHIC REFERENCES: Anderson, N., Burstone, C.J., Weinstein, S. and Koenig, H. 1978. A three dimensional analysis of extraoral traction appliances. J. Dent. Res., 47A: 360. Bert, J.D., Burstone, C.J. and Solonche, D.J. 1978. Experimental analysis of the forces and moments delivered by orthodontic root springs. J. Dent. Res., 57A:363.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$155,998

7.0040, PULSATING FORCES IN ORTHODONTICS

E. Shapiro, Tufts University, Boston Campus, School of Dental Medicine, Dept. of Orthodontics, *136 Harrison Ave., Boston, Massachusetts* 02111 (R01 DE 04487-03)

Currently, most orthodontic systems of mechanotherapy involve the use of heavy continuous forces. Although these have been effective in inducing tooth movement, there has been evidence of trauma, pain, excessive mobility, root resorption and alveolar bone loss. As a consequence the orthodontic profession has desired a more physiologic treatment procedure. The concept presented in this investigation can theoretically achieve tooth movement through a physiologic process involving piezoelectric potential. Current orthodontic techniques preclude this phenomenon from being a factor in treatment.

It is proposed that pulsating forces of the correct magnitude can produce piezoelectric energy that will result in osteoblastic and osteoclastic activity and optimum tooth movement. A force applicator will be designed to produce monophasic pulses of current in the supporting bone. The rate of change of force application will be about twenty times as great as the rate of change of release thereby producing a higher potential of one polarity. This controlled pulsating force on the teeth will produce near unipolar electric potentials in the bone and thereby induce physiologic activity for optimum tooth movement.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $60,254

7.0041, ORTHODONTIC TREATMENT WITH REMOVABLE APPLIANCES

T.M. Graber, American Dental Assn., Health Foundation, *211 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 05307-01)

In the U.S.A. the primary orthodontic treatment procedure utilizes 'external' forces (i.e., multibanded fixed appliances) to achieve treatment goals. In Europe the removable simple plate and functional appliance are the major appliance modalities. Treatment changes are made with 'internal' forces, attempting to harness the natural forces of the orofacial structures. The proposed research will evaluate the therapeutic value of the function corrector of Frankel. One phase of the project will critically examine, over a five year period, the treatment, retention and post-retention changes with the function corrector and compare the results to multibanded fixed appliance therapy. Achievement of treatment objectives and stability of results will be the primary concern. The experimental group (patients 7 to 9 years old with Class II, Division 1 malocculsions) for whom removable appliance therapy is the most appropriate treatment procedure, will be treated with the function corrector utilizing the case selection criteria of Dr. R. Frankel. One control group will consist of patients treated with extraoral force and multibanded fixed appliances. A second control group will be observed but not treated until the emergence of the permanent dentition. A second phase will statistically evaluate lateral cephalometric radiographs and dental casts (1500 records) of patients treated with the function corrector. These records extend over the treatment, retention, and post-retention stages. A third phase will conduct histological and gross studies of periosteal pull, saggital change and condylar growth (after use of a Frankel Corrector) in eight Saimiri Sciureus monkeys.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $93,990

7.0042, PSYCHOLOGICAL AND RADIOGRAPHIC EVALUATIONS OF THE ORTHOGNATHIC SURGERY PATIENT

J.B. Sweet, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Clinical Dental Services Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00213-03 IR)

The psychological and anatomical changes that take place in individuals with middle and lower facial bony defects and malocclusions of the teeth after orthognathic surgery are measured and evaluated. Pre- and post-surgery data obtained by tests, interviews, radiographs, photographs and orthodontic study casts taken at specific time intervals for a period of two years postoperatively are compared.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $20,548

DIAGNOSIS & TREATMENT - SURGERY

7.0043, MECHANISMS OF MUSCLE REATTACHMENT AND MIGRATION

J.A. McNamara, University of Michigan, Ann Arbor Campus, Center for Human Growth & Development, *Ann Arbor, Michigan* 48104 (N01DE52478 (CONTRACT))

This project will provide for studies to determine changes in neuromuscular physiology and craniofacial function due to muscle reattachment, transplantation, and migration with or without osseous surgery, utilizing a young adult primate animal model system to identify and describe stages in muscle adaptation in two types of surgical procedures designed by the Contractor.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $113,179

7.0044, SURGICAL-ORTHODONTICS AND BONE HEALING

W.H. Bell, University of Texas, Health Science Center at Dallas, Southwestern Medical School, Dept. of Surgery, *5323 Harry Hines Blvd., Dallas, Texas* 75230 (R01 DE 03794-07)

The objectives of these studies are to determine how healing takes place following various surgical-orthodontic procedures designed to increase or decrease facial height, delineate what soft tissue is essential to maintain circulation to the mobilized maxillary bone fragments and teeth, determine the effect of soft tissue flap design on circulation to bone and teeth, and study changes in the muscles of mastication. The osseous repair, revascularization, blood flow, stability, electromyographic and histochemical changes in the muscles of mastication, and reinnervation associated with surgical correction of maxillary vertical dysplasias will be studied in 70 adult Rhesus monkeys and selected patients.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$100,256

7.0045, INFLUENCES ON STABILITY FOLLOWING ORTHOGNATHIC SURGERY

W.R. Proffit, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Orthodontics, *Chapel Hill, North Carolina* 27514 (R01 DE 05215-01)

Advances in combined orthodontic and surgical treatment in the past decade have made it possible to correct or significantly improve dentofacial deformities which could not be treated previously. Although the long-term results of orthognathic surgery are stable in most instances, there are some post-treatmnt morphologic changes in almost all patients and significant relapse in a few. The alterations in jaw position and oral cavity volume produced by this surgery require considerable physiologic adaptation. It is likely that the extent of post-treatment morphologic change is related to the degree and pattern of physiologic adaptation. In this project, patients treated in the UNC Dentofacial Clinic will be studied. Morphologic stability will be evaluated and correlations will be sought between post-treatment morphologic changes and: (1) posture of head, mandible and tongue; (2) breathing pattern, as evaluated from nasal air flow and nasal resistance; (3) lip pressures; (4) vertically directed occlusal (biting) forces; and (5) vertically directed tongue forces. Elucidation of these relationships will provide insight into soft tissue function as a factor in the etiology of dentofacial deformity as well as a determinant of post-treatment stability.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$113,901

7.0046, STABILITY OF ORTHOGNATHIC SURGICAL PROCEDURES

R.A. Bays, Medical College of Georgia, School of Dentistry, Dept. of Oral Surgery, *1459 Gwinnett St., Augusta, Georgia* 30902 (R01 DE 05542-01)

This project consists of two phases. The first involves determining the effects of osseous surgery in the mandible and maxilla on the stability of intraosseous metallic implants placed in these facial bones of Cynomolgous monkeys. In this phase a two-directional radiographic technique followed by mathematical triangulation will be utilized to determine implant locations.

In the second phase six monkeys will receive the sagittal splitting osteotomy of the mandible and six will have the three-piece LeFort I maxillary osteotomy for correction of this deformity. Three animals will remain unoperated as controls. The operations will be compared as to dental and osseous stability using the triangulation technique.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$32,052

7.0047, GROWTH AND FUNCTION OF THE MUSCLES OF MASTICATION

D.S. Carlson, University of Michigan, Ann Arbor Campus, Center for Human Growth & Development, *Ann Arbor, Michigan* 48104 (R23 DE 05232-01)

The purpose of this research is to investigate the role of the adductor muscle complex of the mandible in determining the growth and form of the craniofacial skeleton. Emphasis will be placed on (a) defining the normal structure and function of the adductors of the mandible (i.e., the temporalis, masseter and medial pterygoid muscles) and the distribution of bone strain within the craniofacial skeleton as these covary during the growth process in Rhesus monkeys (Macaca mulatta): and (b) determining the interrelationships between muscle function, bone strain and craniofacial form by experimental intervention in the adult.

Analytical techniques will include gross and microscopic anatomy to determine muscle morphology, fiber length and cross-sectional are;

electromyography to determine patterns and intensity of muscle activity; strain gauge analysis to evaluate stress distribution in the craniofacial skeleton in response to jaw function; contractile property analysis to determine, among other variables, length-tension relationships and fatigability; and histochemistry to determine fiber type.

This research on the normal growth and function of the mandibular adductors in sub-adults, and adaptations following experimental intervention of facial form and function in adult monkeys, will provide a foundation for addressing such problems as orthodontic and surgical intervention for correction of gross maxillomandibular disharmonies in growing children.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $37,714

7.0048, LONG-TERM EVALUATION OF SERIAL EXTRACTION IN NAVAJO CHILDREN

C.M. Beck, U.S. Dept. of Health Education & Welfare, Public Health Service, Health Services Admin., Indian Health Service, *Shiprock, New Mexico* 87420 (Y01DE90003 (CONTRACT))

OBJECTIVES AND WORK SCOPE: This 3-month agreement is for Phase I of a bi-phasic 18 month effort to assess the long-term results of serial extraction carried out in a Navajo population 10-12 years ago. Phase is limited to the inventory and catalog of existing records and determination of subject availability. Based upon a review of the completeness of existing records and availability of subjects, the conduct of Phase II will be considered.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $8,885

7.0049, EFFECT OF VARIOUS PREOPERATIVE AND POSTOPERATIVE RINSES ON HEALING AFTER ORAL SURGERY

J.B. Sweet, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Clinical Dental Services Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00241-02 IR)

This clinical study is designed to allow the investigators to evaluate the effectiveness of four different solutions used topically before and after oral surgery procedures. Included will be normal saline solution, the conventional rinse, which will serve as a control. Postoperative localized osteitis and infections will be recorded if they occur, as data, to be considered in the overall evaluation of the use of topical solution for possible prevention of these postoperative problems.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $48,795

DIAGNOSIS & TREATMENT - CRANIOFACIAL GROWTH & REMODELING

7.0050, ANTERIOR DISPLACEMENT OF MAXILLA BY CONTROLLED FORCES

R. Nanda, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Orthodontics, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 03998-05)

The present study is investigating the effect of the application of anteriorly directed forces on the displacement of midfacial bones. The major emphasis of the study is to describe the effect of varying magnitude of force and varying point of force application on the rate and type of displacement. The study is being conducted on young and adult animals as well as freshly killed monkey heads. The monkey heads are being used to study three dimensional primary displacement of various bones to a single force using double-exposure laser inferometry. This information is being used to deliver forces to the live monkeys to obtain predictable displacement of midfacial bones. The changes in the conformation are being evaluated using stereometric x-ray technique and histology. The rate of bone deposition is being studied by tetracycline bone marking. The results of this study will help clinically in delivering force systems to the dentocraniofacial complex which will produce predictable alterations to correct severe malocclusions and certain craniofacial anomalies.

BIBLIOGRAPHIC REFERENCES: Nanda, R.: Protraction of Maxilla in Rhesus monkeys by controlled forces. Am. J. Orthodontics 74:121-141, 1978. Nanda, R.: Differential response of midfacial sutures and bones to anteriorly directed extraoral forces in monkeys. J. Dent. Res. 57:362, 1978 (IADR abstract 01150).

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,

National Inst. of Health,
National Inst. of Dental
Research $42,185

7.0051, INFLUENCE OF ALLERGIC RHINITIS ON FACIAL TYPE

V. Sassouni, University of Pittsburgh, School of Dental Medicine, Dept. of Orthopedics, *C336 Salk Hall, Pittsburgh, Pennsylvania* 15213 (R01 DE 04948-02)

A certain percentage of the population presents with some kind of facial deformity with varied etiologies. Skeletal deformity has been attributed to a variety of factors such as heredity, pathology, trauma and allergy.

The purpose of this project is: 1. To determine if a high incidence of skeletal open bite type and narrow transverse facial dimension exists in patients with perennial allergic rhinitis; 2. To determine the relationship between dentofacial structures, perennial allergic rhinitis and effective nasopharyngeal airway; and 3. To evaluate if the treatment of the respiratory allergic patients at an early age will improve their maxillofacial deformities (in terms of oral and respiratory function and facial dimension).

Facial type will be recorded by means of a standardized lateral cephalometric radiograph and a posterio-anterior radiograph. Facial type will be measured by a number of angular, dimensional and proportional measurements.

The sample will consist of five groups of patients. One group will consist of allergic patients tested for their allergy by skin tests, cutaneous and intracutaneous nasal tests, microscopic and macroscopic blood tests and nasal airway resistance tests, in addition to accurate case histories. This group will have treatment initiated for rhinitis and will be followed for 5 years. A second group of allergic patients will be selected from previous records taken from orthodontic patients. A control group will then be selected from normal healthy children. Two additional subgroups will be derived from the previous three.

The tested allergic group will then be treated for their allergies and it will be determined if an improvement in facial type has followed.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $37,135

7.0052, CRANIOFACIAL VARIATION AND AGING IN THE AMERICAN POPULATION

C.E. Nasjleti, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *2215 Fuller Rd., Ann Arbor, Michigan* 48105 (506-004-F)

A paper entitled 'American Male Population: Age and Race as Factors in Craniofacial Growth' was submitted for publication to the Editor of Journal of Dental Research. The present investigation is based on cephalometric data obtained from the Veterans Administration Medical Center in Ann Arbor, Michigan. Two groups of individuals are involved. The first group consists of a total of 244 black adult males ranging in age from 20 to 80 years; the second group consists of 1039 white males in the same age range. Both groups were seen for care at the VAMC, but were selected to be otherwise representative of the American adult male population, i.e., only patients with 'normal' medical histories were included in the study. Each were dentulous and had a sufficiently natural occlusion, with anterior and posterior centric stops, so that the measurements considered could be reliably determined in centric occlusion. The measurements reported here are defined in terms of the coordinate points of Walker and Kowalski, as reported in previous papers from this laboratory.

RESULTS: Age and race have been identified as important factors in the analysis of data on craniofacial morphology and development. In the American black and white populations, a number of craniofacial dimensions continue to change throughout adulthood and both size and shape measurements may differ in the two racial groups at any age. Applications in orthodontics and prosthetic dentistry are indicated.

SUPPORTED BY

U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

DIAGNOSIS & TREATMENT - JAW MOVEMENT ANALYSIS

7.0053, FUNCTIONAL DISTURBANCES OF THE MASTICATORY SYSTEM

M.M. Ash, University of Michigan, Ann Arbor Campus, School of Dentistry, *Ann Arbor, Michigan* 48104 (P50 DE 02731-130001)

This research relates to the development of diagnostic and treatment methods for the solution of dental problems such as functional temporomandibular joint muscle-pain disturbances, acute and chronic TMJ arthritis, bruxism, and trauma from occlusion. Methods involve measurements of electromyography and jaw motion, coupled with clinical observations. The measurement of EMG and jaw motion is centered around the acquisition and analysis of data by minicomputer. A clinical index, based on an ordinal quantification of signs and symptoms, is used and data analyzed by non-parametric statistical methods. Significant results are being obtained from the jaw motion phase-plane technique and from EMG silent period activities.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $119,294

7.0054, CRANIOFACIAL ARTICULATIONS AND MASTICATORY FUNCTION

B.C. Moffett, University of Washington, School of Dentistry, Dept. of Orthodontics, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (R01 DE 02931-12)

The long-term objectives are to make correlated studies of facial form and masticatory function in the presence of experimental variables, and to formulate from these studies new concepts for the diagnosis and treatment of severe malocclusion and jaw dysfunction. Alterations of facial growth and masticatory function will be produced experimentally in monkeys by means of mechanical forces and experimental brain lesions. Documentation of changes in form will be cephalometric and histologic; function will be studied by mandibular tracking combined with EMG analysis.

BIBLIOGRAPHIC REFERENCES: Kokich, V., Shapiro, P., Moffett, B., and Retzlaff, E. (Chapter) Age changes in facial sutures, in book Aging in Nonhuman Primates edited by Douglas Bowden, Raven Press, 1978. Smith, R. Bone dynamics associated with the controlled loading of bioglass coated aluminum oxide endosteal implants. Am. J. Orthod. In Press. 1978. (This article will be awarded the American Association of Orthodontics research prize for 1978.)

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

7.0055, INVESTIGATION OF FUNCTIONAL MANDIBULAR MOVEMENTS

C.H. Gibbs, State University System of Florida, University of Florida, School of Dentistry, Dept. of Basic Dental Sciences, *Gainesville, Florida* 32601 (R01 DE 04157-06)

Instrumentation and computer capabilities that measure, record, display and duplicate preconscious jaw movements have been developed. This Replicator system provides a basis for objective study and evaluation of occlusion. A partial listing of parameters investigated includes paths of movement of the central incisor, condyles and molars; instantaneous centers of rotation; and velocity characteristics of jaw movements.

A data base for adult subjects with good occlusion and specific malocclusion has been established and it is proposed to record young subjects in their growth and development period. These data enhance the basic understanding of the neuromuscular control and guidance of the jaw.

An objective of this research is to provide specifications for restorative dentistry by categorizing condylar border movement pathways from two independent studies: 1) Replicator-electronic method and 2) Lee System--engraving method. Preliminary studies show that jaw movement analyzers and articulator controls used in fixed and removable prosthodontics would be greatly simplified.

Patients in dysfunction, patients undergoing treatment and normal patients modified with the insertion of restorations with known occlusal interferences are being studied in relation to diagnosis of dysfunction and treatment evaluation. The recorded data will provide basic criteria for evaluation: 1) occlusal disharmonies; 2) TMJ disorders and 3) muscle dysfunction.

These studies will lead to an improvement of dental treatment services as they relate to occlusion.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $91,807

7.0056, PHYSIOLOGICAL STUDIES OF MASTICATION

T. Gay, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Oral Biology, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 04610-01A2)

The major objective of the research proposed in this application is to provide both quantitative and interpretive accounts of the complex movements of the mandible, and the motor patterns that underlie those movements, during the masticatory cycle of normally dentate human subjects.

A second objective of the proposed research is to apply our experimental techniques to the masticatory functioning of patients with malocclusion, and myofascial pain and temporomandibular joint dysfunctions.

Our experimental approach to these objectives is the use, in combination, of the techniques of electromyography and magnetometer tracking. Relationships between movement parameters (position and velocity) and muscular forcing functions (muscle action potentials) will be established by computer aided analysis involving cross-correlation and EMG ensemble averaging techniques.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$54,084

7.0057, DENTAL SIGNIFICANCE OF JAW MUSCLE SILENT PERIODS

W.D. McCall, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Medicine, *3435 Main St., Buffalo, New York* 14214 (R01 DE 04889-02)

Pain and dysfunction associated with the temporomandibular joint (TMJ) and the muscles of mastication have produced conflicting etiological theories and diverse treatment modalities. The controversy may be due in part to the lack of either observable pathology or definitive diagnostic signs. The electromyographic silent period may provide such a sign and perhaps some insight into the etiology.

The silent period is a brief pause in the electrical activity of muscle in the midst of an otherwise sustained, voluntary contraction. The mean duration of the silent period is greater in a group of TMJ dysfunction patients than in a group of asymptomatic subjects. The purpose of our research is to investigate both the clinical utility of the electromyographic silent period and the basic mechanisms underlying its generation.

Current results suggest that level of voluntary activity is not a determining factor in jaw muscle silent period duration although it is in limb muscles, that silent period duration increases with increased symptom severity, and that dental interventions such as immediate complete dentures and rapid palatal expansion can cause a significant increase in silent period duration.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$39,169

7.0058, JAW MOVEMENTS AND RELATED MUSCLE ACTIVITIES IN MAN

P.E. Mahan, State University System of Florida, University of Florida, School of Dentistry, Dept. of Basic Dental Sciences, *Gainesville, Florida* 32601 (R01 DE 04924-02)

This project proposes to demonstrate any difference in activity of the superficial and deep layers of the masseter and temporalis muscles correlated with different phases of the masticatory stroke and biting force.

It will determine whether or not the human inferior belly of the lat. pterygoid contracts on jaw depression and the superior belly contracts on jaw elevation as demonstrated in the Rhesus monkey.

It will also demonstrate the pattern of lat. pterygoid and inferior belly activity during dysfunction of the TMJ meniscus, i.e., meniscus-condyle discoordination with joint records.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$17,203

7.0059, THE PLANE OF OCCLUSION

H.R. Kolb, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Kecoughtan, Hampton, Virginia* 23667 (590-001-P)

The objective of this project is to determine whether or not there is one 'optimum' orientation of the plane of occlusion that will function harmoniously within a given mandibular movement pattern. The technique involves making pantographic tracings of a subject's mandibular movements and transferring the recordings to an articulator capable of reproducing said movements. The sixth subject was discharged from the domiciliary before work could be completed. Work on a seventh subject has not yet commenced.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

DIAGNOSIS & TREATMENT - TOOTH ATTACHMENT & DISPLACEMENT

7.0060, OSTEOCLAST ORIGIN AND HISTOGENESIS IN PERIODONTIUM

W.E. Roberts, University of the Pacific, School of Dentistry, Dept. of Orthodontics, *San Francisco, California* 94103 (R01 DE 05136-01)

The role of local peridontal ligament (PDL) cells, peripheral monocytes, and in situ macrophages in the origin and histogenesis of osteoclasts along a previously resorbing alveolar bone surface will be investigated in 6-8 week old rat PDL. The nuclei of circulating monocytes will be selectively labeled with 3H-thymidine (3H-Tdr), and the cytoplasm of the PDL macrophages labeled by intravenous injection of a carbo particle suspension. Computerized histomorphometry of autoradiographs of 3 microns serial sections will categorize all cells according to cell type, geographic location (zone), nuclear volume, autoradiographic grain count, and presence or absence of carbon particles. Dynamics of these cellular parameters will be studied during stimulation of osteoclast histogenesis with parathyroid extract (PTE) or biomechanical induction (accelerated approximal drift). A kinetic model for osteoclast histogenesis will be derived.

An important aspect of this study is the development of a digitizer-minicomputer-plotter system for automated quantitation and data processing of cell kinetic parameters of bone histomorphometry. This will open new horizons for investigating the interaction of DNA synthesis, mitosis change in nuclear volume, influx of hematogenous cells, and cell migration patterns associated with bone cell histogenesis. In conjunction with tetracycline labeled iliac crest bone biopsies incubated in 3H-Tdr, the proposed computerized methods could evolve into a powerful clinical tool for diagnosing and evaluating treatment of skeletal disease. A more direct dental application would be as an in vivo PDL model for investigating the biological response of biomechanically defined force systems.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $78,828

VIII. ACQUIRED MALRELATIONS & ACCIDENT CASES

PATHOLOGY

8.0001, CONDYLECTOMY AND ANTERIOR POSITIONING OF THE MANDIBLE

V.M. Bakker, Harvard University, Boston Campus, School of Dentistry, Dept. of Orthodontics, *188 Longwood Ave., Boston, Massachusetts* 02115 (R23 DE 05540-01)

Regeneration after removal of healthy mandibular condyles has been observed in humans, primates, and rats. The process of regeneration is not completely understood and contributing factors have not been isolated. The proposed study will provide insight into the complex phenomenon of regeneration after condylectomy and the factors that may contribute to it. This will be done by displacement of the mandible anteriorly thus preventing the posterior and inferior collapse observed after condylectomy in the human and the Rhesus monkey.

The mandible is a dominant morphological and functional characteristic of the face. Displacement of the mandible with changed muscle action and skeletal adaptations is used in the human for treatment of facial growth discrepancies. The exact action of this applied force is not known. However, it may influence the mandibular condyle which is a main growth site in the mandible.

The purpose of this study is twofold: 1. Identification of the importance of mandibular displacement in the process of mandibular condyle regeneration after condylectomy. 2. Determination of the role of the mandibular condyle in reacting to applied forces in the mandible. Bilateral condylectomies will be performed in growing Rhesus monkeys. Half of these monkeys will receive an appliance to displace the mandible anteriorly. Identical appliances will be placed in monkeys without condylectomies. After one year all animals will be sacrificed.

The evaluation method will include: Longitudinal radiographs with implants as reference points, plaster models, and histological methods.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $12,150

DIAGNOSIS & TREATMENT

8.0002, THE EFFECT OF EPIDERMAL GROWTH FACTOR ON PALATAL WOUND HEALING

J.G. Webb, U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research, *Washington, District of Columbia* 20012 (DA0G6049)

The oral cavity is subject to trauma from a variety of sources. healing of many oral tissue wounds requires epithelial growth. A protein termed 'epidermal growth factor' (EGF) has been isolated from the submaxillary glands of rats and studied mostly in vitro. The objective of the present study is to determine the ability of EGF to accelerate the healing of palatal wounds in rats.

Control and experimental animals will receive palatal wounds using a punch biopsy instrument. Experimental animals will be treated with EGF injections at the wound site at the time of wounding and twice daily until sacrificed. Controls will be similarly injected with physiological saline. Healing will be evaluated by a determination of the area of epithelial fill in the wounds and histologic examination.

SUPPORTED BY

U.S. Dept. of Defense, Army,
Medical Research &
Development Command, Inst.
of Dental Research funds n.a.

8.0003, NEW AND IMPROVED TECHNIQUES FOR GRAFTS AND BONE REGENERATION IN TRAUMATIC WOUNDS

E.A. Russell, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Surgery, *Washington, District of Columbia* 20012 (DA0H6037)

To develop simple, rapid methods of soft tissue or bone grafting of particular interest to the oral surgeon treating combat type maxillofacial injuries.

The fate, metabolism, osteogenic potential and tissue compatibility of ceramic and copolymer materials will be studied alone and in combination. The application of these materials to avulsive type wounds in both animals and humans will be pursued.

SUPPORTED BY

U.S. Dept. of Defense, Army,
Medical Research &
Development Command, Inst.
of Dental Research funds n.a.

8.0004, EVALUATION OF HEALING OF TRAUMATIC BONE FRACTURES AND OF BONE GRAFTS

R.G. Triplett, U.S. Dept. of Defense, Defense Nuclear Agency, Armed Forces Radiobiology Research Inst., *Bethesda, Maryland* 20014 (DH090301)

(A) Evaluate bone graft healing with radionuclide techniques, (B) Check the effect of anemia in graft healing, (C) Determine how radiation effects this model.

Full-thickness mandibular defects are surgically created in Beagle dogs and replaced by allogeneic xenogeneic or composite bone grafts. Bone imaging is performed serially over 2 months post grafting using Tc-99m-stannous diphosphonate and gamma camera - computer system. The pattern of activity in the graft is compared to that of the host bone. this is a collaborative effort with Navy Medical Research Institute investigators.

SUPPORTED BY

U.S. Dept. of Defense, Defense
Nuclear Agency, Armed Forces
Radiobiology Research Inst. funds n.a.

8.0005, LONG-TERM STUDIES OF RECONSTRUCTION AND REHABILITATION IN NAVY AND MARINE CORPS ORAL AND MAXILLOFACIAL CASUALTIES AND INJURIES

R.G. Triplett, U.S. Dept. of Defense, Navy, Naval Medical Research Inst., Clinical Sciences Div., *Bethesda, Maryland* 20014 (DN840239)

TECHNICAL OBJECTIVE: Ten to fifteen percent (30,000-45,000 in Vietnam) of all battle casualties sustain oral and maxillofacial injuries. These wounds require long periods of hospitalization and complex surgery. This study is designed to delineate the major problems involved in long-term rehabilitation and to address the most important aspects through scientific research. It is anticipated that this information will lead to improved treatment of these injuries thereby shortening reconstruction time and minimizing the loss of military man-hours.

APPROACH: Complete case histories will be maintained and updated on selected maxillofacial casualties with emphasis on those in which there is extensive hard and soft tissue damage requiring lengthy treatment. Follow-up information will be obtained through periodic clinical examination and data questionnaires. During the present phase of the study a biographical inventory will be developed as an initial step in determining the degree of adaptability these patients have achieved over the years post-injury. This data will be used to develop a psychological test to determine the psychological changes resulting from maxillofacial war wounds. Two groups of matched controls will include Vietnam veterans 1. with no injuries and 2. with injuries in other anatomical locations.

PROGRESS: A textbook dealing with surgical management of maxillofacial war wounds has been published. This will be of direct benefit for military professionals in the event of another armed conflict. One publication - textbook, 303 pages.

SUPPORTED BY

U.S. Dept. of Defense, Navy,
Naval Medical Research &
Development Command,
National Naval Medical Center funds n.a.

IX. RESTORATIVE MATERIALS & PROSTHESES

DIAGNOSIS & TREATMENT - RESTORATIVE FILLING MATERIALS

9.0001, DEVELOPMENT AND IMPROVEMENT OF METALLIC RESTORATIVE MATERIALS (09)

E.F. Huget, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Dental Materials, *Washington, District of Columbia* 20314 (DA0G6034)

Annual army expenditures for precious metals utilized in the fabrication of fixed dental prostheses are in the vicinity of $1,000,000. The cost of an equal volume of base metal alloy is $30,000. Properties of base metal alloys indicates however, that these alloys cannot be utilized for small castings without drastic metallurgical modifications. This work is therefore being conducted to: (a) develop heat treatment methods for controlling properties of nickel-chromium based casting alloys and (b) evaluate nickel-chromium based alloys for use in operative dentistry.

The properties of nickel-chromium based alloys will be studied in detail by the various physical methods available in order to devise procedures which will optimize their usefulness. Any improvement obtained will be evaluated clinically.

SUPPORTED BY

U.S. Dept. of Defense, Army,
Medical Research &
Development Command, Inst.
of Dental Research — funds n.a.

9.0002, STRUCTURE AND PROPERTIES OF ACRYLIC POLYMERS

R.P. Kusy, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Orthodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130114)

The purpose of this investigation is to understand the relationship between the chemical or microscopic structure and the physical properties in 2-phase acrylic polymers. Three similar classes of materials are under study: the denture base and anterior restorative acrylics, the cranio-facial materials, and the orthopedic cements. Using both conventional and novel techniques, evaluations are made on four levels: (1) pre-mix and post-mix characterization (molecular weight, particle geometry, gel/sol partition); (2) the application technique; (3) morphology (surface and fracture); and (4) physical properties (tensile strength, fracture surface energy, inherent flaw size). To reduce the complexity inherent in the 2-phase acrylics, work is also conducted on 1-phase poly(methyl methacrylate) and on mixtures of methacrylate monomer with a crosslinking agent.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research — $12,573

9.0003, IN SITU REPLICATION TECHNIQUE AND THE WEAR OF RESTORATIVE MATERIALS

R.P. Kusy, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Orthodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130123)

With the aid of the scanning electron microscope (SEM) the feasibility of replicating specific tooth surfaces in situ is being assessed. A variety of materials have been screened using a number of preparation techniques to determine which candidate has the best resolution, depth of detail, reproducibility, and processing characteristics. With this in situ replication technique, problems related to the wear of restorations, marginal integrity, and cavity preparation will be examined.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research — $20,118

9.0004, CLINICAL EVALUATION OF RESTORATIVE MATERIALS AND TECHNIQUES

K.F. Leinfelder, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Operative Dentistry, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130191)

The purpose of this study is two-fold. The first part consists of clinical evaluations of restorative materials and techniques. The sub-task projects included in this part of the investigation are as follows: Long term evaluation of proprietary and experimental high copper containing amalgams, modified cavity preparations for composite resins, burnishing and finishing techniques for amalgam restorations, as well as proprietary and experimental composite resins in posterior teeth. The second part consists of developing objective criteria that can be used to determine the clinical performance of a wide range of restorative materials over varying lengths of time.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$69,403

9.0005, CLINICAL BEHAVIOR OF DENTAL RESTORATIVE MATERIALS

D.B. Mahler, Oregon State Higher Education System, University of Oregon Health Sciences Center, School of Dentistry, Dept. of Dental Materials Science, *611 S.W. Campus Dr., Portland, Oregon* 97201 (R01 DE 02320-14)

The basic objective of the proposed research is to provide information leading to the improvement of dental amalgam. This will be accomplished by establishing relationships between clinical performance, laboratory tests, and metallurgical characteristics. Once these relationships are established, a rational modification of amalgam systems can be undertaken to improve the clinical performance of this important restorative material.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$64,789

9.0006, MARGINAL FRACTURE OF DENTAL AMALGAM

D.B. Mahler, Oregon State Higher Education System, University of Oregon Health Sciences Center, School of Dentistry, Dept. of Dental Materials Science, *611 S.W. Campus Dr., Portland, Oregon* 97201 (R01 DE 02936-11)

The objective of the proposed work is to provide information leading to the development of improved dental amalgam. The approach will be to identify microstructural features of dental amalgams for which clinical performance characteristics have been determined on a companion project. A correlational analysis will be applied to determine which microstructural features are most desirable and the mechanisms whereby amalgam structures can be optimized. Methods of analysis will include electron microprobe analysis, xray diffraction and optical metallography.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$48,594

9.0007, WEAR OF COMPOSITE RESTORATIVE RESINS

J.M. Powers, University of Michigan, Ann Arbor Campus, School of Dentistry, Dept. of Dental Materials, *Ann Arbor, Michigan* 48104 (R01 DE 03416-08)

The mechanism of wear of commercial and experimental formulations of composite restorative resins will be studied in the laboratory by a two-body abrasion test and a single-pass sliding test. Also, the wear of two commercial composites (one with glass filler and one with quartz filler) and an amalgam will be evaluated clinically in Class I restorations in human patients over a three-year period. In the laboratory phase, the effect of the resin matrix, silane coupling agent and inorganic reinforcing agent on the abrasion resistance of experimental composites will be studied. The objectives of the clinical study are to evaluate a methodology for quantitative assessment of clinical abrasion in posterior teeth, to correlate clinical abrasion with laboratory studies, and to obtain a comparative analysis of the wear rate of three commercially available restorative materials. The information should be useful in improving the wear resistance of composite restorative materials.

BIBLIOGRAPHIC REFERENCES: Roberts, J. C., Powers, J.M., and Craig, R.G. Wear of dental amalgam. J. Biomed. Mater. Res., 11(4):513-23, 1977.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$78,102

9.0008, A CLINICAL STUDY OF DENTAL MATERIALS AND TECHNIQUES

D.K. Warfield, Emory University, School of Dentistry, Dept. of Operative Dentistry, *106 Forest Ave. N.E., Atlanta, Georgia* 30303 (R01 DE 03504-10)

The final year of this grant will involve a comparison of amalgams, composites and silicates that were placed under controlled conditions. As many patients as possible will be recalled and the restorations evaluated for marginal integrity, recurrent decay, corrosion and color stability. In a concurrent and more recent study, amalgam restorations were inserted next to previously placed inlays, then the sequence of placement was reversed. These patients will also be recalled and the changes recorded.

All patients will be evaluated using Ryge criteria supplemented with 6X magnification color photographs. All clinically unacceptable restorations will be replaced and those removed will be analyzed with x-ray diffractions and electron probe in an attempt to evaluate any differences in corrosion products.

All patients will be given an extensive dietary survey and these results analyzed by computer to determine if any correlation between diet and corrosion/staining can be established. Finally, a series of laboratory experiments involving impression materials, amalgams, handpieces and other biomaterials will be continued.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$46,681

9.0009, EFFECT OF CORROSION ON DENTAL AMALGAMS

M. Marek, Georgia Inst. of Technology, School of Engineering, *225 North Ave. N.W., Atlanta, Georgia* 30332 (R01 DE 03601-07)

Deterioration of dental amalgams due to electrochemical reactions will be studied in vitro. The mechanism of the corrosion attack, and the effects of corrosion on the properties of various types of amalgam will be investigated. The main emphasis will be on the determination of the corrosion behavior of high copper amalgams, which exhibit higher corrosion resistance than conventional amalgams but have been shown to suffer in some cases deterioration by an unknown mechanism. Other studies will include determination of the effects of corrosion on the mechanical properties of various types of dental amalgam, investigation of the relationships between porosity, mercury content, and corrosion, and examination of the effects of aging on the corrosion properties. Corrosion test methods and conditions used in the studies of dental amalgams will be examined and evaluated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$41,844

9.0010, PROPERTIES OF HIGH COPPER CONCENTRATION AMALGAMS

E.H. Greener, Northwestern University, Chicago Campus, School of Dentistry, Dept. of Biological Materials, *Chicago, Illinois* 60611 (R01 DE 03637-05)

The proposed research is designed to determine the relationship between amalgam alloy formulation, creep and other mechanical properties, corrosion resistance and microstructure of Cu-rich amalgams. Saline and sulfide corrosion resistance of new and experimental amalgams will be evaluated as well as steady state creep parameters and axial tensile stress-strain relationships. Clinical retrieval studies will attempt to relate ongoing in vivo processes with in vitro phenomenon produced in model systems. Alteration of microstructure resulting from these investigations will be determined by scanning electron microscopy and energy dispersive x-ray analysis (qualitative and quantitative analysis of compositional variations). Synergistic effects of corrosion, creep and alloying modifications will be investigated via corrosion-creep testing and systematic alloying variations to produce distinctive amalgams with potential for superior clinical performance.

BIBLIOGRAPHIC REFERENCES: Larson, T.H., Sabott, D., Cooley, R. and Greener, E.H.: A Clinical Study of Marginal Integrity and Tarnish Behavior of Three Cu-Rich Amalgam Systems. J. Oral Rehab. 6: 61-66, 1979. Lautenschlager, E.P., Szurgot, K. and Greener, E.H.: Time-Temperature Relationship for Creep of Amalgam. Presented at LADR, New Orleans, March, 1979. Abstract No. 25.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$61,103

9.0011, DENTAL RESINS THAT EXPAND ON POLYMERIZATION

V.P. Thompson, University of Maryland, Baltimore Professional Schools, School of Dentistry, Dept. of Basic Dental Sciences, *66 W. Baltimore St., Baltimore, Maryland* 21201 (R01 DE 03869-04)

Unsaturated spiro orthocarbonates (SOC) synthesized in these laboratories exhibit polymerization expansion. These crystalline monomers can be made to free radical polymerize.

Fine crystals of dimethylene spiro orthocarbonate can be mixed with thinned BIS-GMA based resins to form a comonomer mixture. Polymerization of the SOC lags that of the BIS-GMA unless temperatures above 50 degrees centigrade are employed. Current research is exploring methods to increase the rate of polymerization of the SOC in order to optimize the expansion (4.5 percent R.T.)

of these monomers. Cationic catalyst systems (SnF4 or SnCl4) used in parallel with amine: peroxide systems are being employed. Eutectic mixtures of various SOC monomers will be utilized to reduce the melting temperature of the crystal to increase R.T. polymerization rates. Physical testing involves tensile and compressive strength and tooth adhesion studies employing thermal cycling are conducted on these dental copolymers.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

9.0012, A STUDY OF REINFORCEMENTS IN DENTAL COMPOSITES

F.E. Wawner, University of Virginia, School of Engineering & Applied Science, Dept. of Materials Science, *Garrett Hall, Charlottesville, Virginia* 22903 (R01 DE 03925-05)

The objective of this program is to perform a study on the influence of reinforcement materials on the properties of dental composite restoratives. This will be accomplished by making a systematic study of the influence of shape, size, and type. Specifically, the use of shaped particle fillers, such as flakes and fibers with favorable length to thickness ratio, as compared to other regular or irregular particles, will be investigated to attain formulas for optimal dental requirements. Much information has been developed in other technological areas showing the superiority of two dimensional reinforcements (flakes/fibers) in composite materials over other configurations (i.e. spherical or irregular shaped particles) and with regard to strength, modulus, water sorption, wear resistance, and dimensional stability. It should be possible to apply this knowledge to obtain a vastly improved dental composite restorative system. This study involves treating the two dimensional reinforcing filler particles, determining methods for optimum orientation of the reinforcement in the composite system, fabricating appropriate test specimens, and conducting a complete evaluation of the composite system.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$46,909

9.0013, DENTAL ALLOY WITH SMALL ADDITIONS OF OTHER MATERIALS

L.B. Johnson, University of Virginia, School of Engineering & Applied Science, Dept. of Materials Science, *Garrett Hall, Charlottesville, Virginia* 22903 (R01 DE 03965-06)

The presence of about 1-2% Zn in a Ag-Sn amalgam has been shown to have about a 10 fold effect upon the early compressive strength and the creep. The objective of this research is to understand and improve the properties of dental amalgams by observing the effects of additions of numerous individual materials.

Standard, ADA approved tests will be used to observe the effects of these additions on properties related to clinical usage.

Location of the small amounts of materials will be made by an analytical electron microscope (STEM) and a SEM with dispersive analyzer. X-ray diffraction will aid in the determination of structure and structure changes.

Alloys will be prepared both by splat cooling and lathe cutting so as to compare the methods.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$65,361

9.0014, HYDROPHOBIC FLUORINE-CONTAINING RESTORATIVE POLYMERS

R.G. Craig, University of Michigan, Ann Arbor Campus, School of Dentistry, Dept. of Dental Materials, *Ann Arbor, Michigan* 48104 (R01 DE 04050-03)

Polymers containing fluorinated side chains and also containing unsaturated groups available for crosslinking will be synthesized. The polymer can be crosslinked by free radical polymerization and would result in a restorative material with sufficient hydrophobicity to prevent capillary penetration between a tooth and the material. The wettability of the polymers will be determined by contact angle measurements and the ability for liquids to penetrate between the polymers and tooth will be assessed by neutron activation analysis. Promising hydrophobic polymers will be used to prepare composites and their physical and mechanical properties will be determined and their wear resistance evaluated.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,

National Inst. of Dental
Research $0

9.0015, AMALGAMATION KINETICS ON AG-SN (X) ALLOYS

T. Okabe, Medical College of Georgia, School of Dentistry, Dept. of Restorative Dentistry, *1459 Gwinnett St., Augusta, Georgia* 30902 (R01 DE 04262-05)

The objective of this project is to improve high copper dental amalgams by studying (1) amalgamation kinetics and (2) amalgam structure and properties. In the kinetics research, radioisotope techniques are being used to study dissolution rates of high copper aloys into mercury. These techniques will also be used to measure the growth rate of the amalgam matrix phase, gamma-one, in alloys with several different compositions. In the amalgam structure and property research, compressive strength and ADA creep are being measured in a variety of amalgams aged for up to one year at 37-degrees C. In addition, mechanical property data on high copper amalgams are being correlated to data on the volume fractions and grain sizes of the phases present in these amalgams. Microstructural changes occurring during creep deformation are being followed with a recently installed scanning electron microscope. This microscope and the attached x-ray analysis equipment have already yielded significant information about creep and fracture in amalgam. Extensive microstructural analysis of two phenomena associated with creep, grain boundary sliding and a newly discovered 'needle' phase, are being conducted. Work is also proceding on a 'chewing machine' which will be desinged to produce in vitro marginal fracture of amalgam restorations. Examination of these marginal fractures using the scanning electron microscope should lead to increased understanding of the relation between creep deformation and marginal fracture.

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SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $75,500

9.0016, CREEP AND EVALUATION TECHNICS OF AMALGAM FAILURE

R.W. Phillips, Indiana University, Indiana University - Purdue University at Indianapolis, School of Dentistry, Dept. of Dental Materials, *1121 W. Michigan St., Indianapolis, Indiana* 46202 (R01 DE 04367-04)

The primary objective of this research is to secure more definitive information on the validity of the property of creep in predicting the susceptibility of amalgam restorations to marginal breakdown. Considerable evidence exists that does indicate a positive correlation between that property and the marginal deterioration of clinical restorations. However, the high and low creep alloys used in those studies have differed from each other with respect to composition, particle size and configuration and, undoubtedly, heat treatment. Thus, a number of variables existed in addition to creep and the question arises as to whether the observed relationship between creep and marginal breakdown is valid for amalgam in general or merely coincidental for those systems. Recent work by this laboratory reveals that the creep of certain alloys can be altered markedly by trituration time. Therefore, in this study it is proposed to eliminate the aforementioned variables by placing paired restorations of a single alloy with widely different creep values, achieved by control of trituration time. The restorations will be monitored for marginal discrepancies over a 3 year period. There is no doubt that one of the real problems in research of this nature is the methodology utilized in the evaluation of the clinical restorations. Several procedures have been or are being employed and it is possible that some of the divergent results emanating from different clinical studies stem from differences in the evaluation criteria and technics. Thus, a second objective of this investigation is to assess the evaluation procedures. All of the restorations will be evaluated at each examination period by 7 recognized technics and the results collated.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $28,559

9.0017, PIN AND SLOT RETENTION IN AMALGAM AND COMPOSITE MATERIAL

W.C. Outhwaite, Medical College of Georgia, School of Dentistry, Dept. of Dental Materials, *1459 Gwinnett St., Augusta, Georgia* 30902 (R01 DE 04394-03)

The purpose of this investigation is to ascertain if small slots cut with inverted cone burs are an acceptable alternative to the presently used threaded pins in the restorative treatment of badly broken down teeth. To achieve this purpose it has been necessary to design and make a machine that will apply simulated chewing stresses to extracted teeth that have been restored with dental amalgam and composite resins.

Such a machine has been built, and the necessary transducers to measure strain in the restorations under test.

Investigation of the optimum slot design has shown that the smallest slot that can be cut with dental burs is the best. Slots cut with the 033 1/2 bur are ideal and a greater strength per unit area is obtained in the restorative material with these than when larger slots are used.

Initial results in the study using the new simulated chewing machines indicate that the slots are comparable with pins as a retentive mechanism.

When the laboratory phase of this study is completed a clinical study is planned.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$11,980

9.0018, CORROSION AND CLINICAL BEHAVIOR OF DENTAL AMALGAM

G. Ryge, University of the Pacific, School of Dentistry, Dept. of Fixed Prosthodontics, *San Francisco, California* 94103 (R01 DE 04516-03)

OBJECTIVES: 1. To complete one year evaluations on all patients, using the USPHS (Ryge) and Mahler criteria. 2. To perform two year evaluations on all patients, using the USPHS (Ryge) and Mahler criteria. 3. To compile the photogrammetric data, and to make stereophotogrammetric measurements of the restorations in the 10 patients, at baseline and at three month intervals thereafter. 4. To complete storage of patient and evaluation data in the computer at the U.O.P. site; and continue update at O.R.U. 5. To compare the two clinical evaluation systems and to correlate with the stereophotogrammetric system. 6. To establish electrochemical corrosion parameters with a close correlation with the clinical performance of the alloys.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$79,790

9.0019, AMALGAM - IMPROVED ALLOY AND MANIPULATION TECHNIQUES

N.W. Rupp, American Dental Assn., Health Foundation, Research Unit, *211 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 05029-02)

This study is designed to elucidate measures to increase the serviceable life of dental amalgam restorations. In this fifth year of the project five-year-old restorations are being observed for margin integrity, contour and surface texture. Concurrently, laboratory tests are being made and the data correlated with the clinical observations. The laboratory data include measurements of physical properties such as dimensional changes during hardening and over 2 and 3 years in varying storage temperatures. Some dimensional change specimens are unrestricted and others are in cavities. Unrestricted specimens have wide range of dimensional changes which seem to be related to composition of the alloy and also time and temperature related phase changes.

The same brands and batches of amalgams confined to cavities do not have expansions similar to the unrestricted specimens but are directly related to their individual creep values. The causes of this phenomenon are being studied by chemical, x-ray diffraction, metallographic and electron probe procedures. The results should give clues to further composition changes and techniques of manipulation which should improve amalgam restorations, and through these, to better dental health.

BIBLIOGRAPHIC REFERENCES: Paffenbarger, G.C., Rupp, N.W. and Patel, P.R. High Copper Content Amalgams: Linear Dimensional Change after Storage in Air for 65 Weeks at 60, 37 and 23 degrees C. J. Dent Res 57: Special Issue A, Abstract 0193, Jan 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

9.0020, CREEP AND CORROSION OF DENTAL AMALGAMS

N.K. Sarkar, Louisiana State University, Medical Center, School of Dentistry, Dept. of Biomaterials, *1542 Tulane Ave., New Orleans, Louisiana* 70112 (R01 DE 05126-02)

The objective of this investigation is to analyze, assign and clarify the controversial roles of creep and corrosion in the marginal breakdown of dental amalgams of conventional chemistry. The methodology will involve the determination of the creep and corrosion behavior of dental amalgams as a function of the nature and volume fractions of various microstructural phases with special emphasis on the ratios of gamma 1/gamma 2 and gamma 1/gamma 2 plus CuSn in the matrix of amalgams fabricated from alloys of known chemical composition and processing history. Creep data as a function of stress and temperature will be obtained with a creep tester. Corrosion data will be obtained using potentiostatic anodic polarization techniques. Microstructural characterization will be carried out using optical microscopy, scanning electron microscopy, x-ray diffraction analysis and electron probe microanalysis. The results will be interpreted in terms of the creep and corrosion behavior of the individual phases, singly and in combination.

Conclusions will be made regarding specific relationships between microstructure and creep and corrosion. It is anticipated that a relevant predictive parameter for the marginal breakdown of dental amalgams will be established.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $44,791

9.0021, IMPROVEMENT OF PREVENTIVE AND RESTORATIVE MATERIALS

R.L. Bowen, American Dental Assn., Health Foundation, *211 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 05129-02)

The objectives of the project are the conception, synthesis, and development of improved materials for use in preventive and restorative dentistry.

An attempt will be made to develop means to remove the 'smeared' layer (the disturbed surface layer formed when cutting, scraping, or polishing of dentin or enamel is done with mechanical instruments) by means that will not threaten the health of the vital pulp. Also, chemical treatments of dentin and enamel surfaces with 'mordants' will be evaluated to determine if they can improve the quality of active sites to which polyfunctional surface-active comonomers can adhere.

Certain mordant metal ions can rapidly exchange with calcium ions on hydroxyapatite surfaces, and can probably interact with collagenous components of dentin also. It will be important to learn if these bound metal ions can react also (subsequently) with chelating groups of the coupling agents, and these agents, in turn, copolymerize with monomers of sealants, composites or other dental resins.

BIBLIOGRAPHIC REFERENCES: Misra, D.N., and Bowen, R.L.: Sorption of Water by Filled Resin Composites, J Dent Res 56(6): 603-612, 1977. Antonucci, J.M. and Bowen, R.L.: Adhesive Bonding of Various Materials to Hard Tooth Tissues: XIII. The Synthesis of a Polyfunctional Surface-Active Amine Accelerator, J Dent Res 56: (8):947-942, 1977.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $107,609

9.0022, A MICROSCOPIC AND CLINICAL STUDY OF CERVICAL EROSION

A.J. Gwinnett, State University of New York, Health Science Center at Stony Brook, School of Dentistry, Dept. of Oral Biology & Pathology, *Stony Brook, New York* 11790 (R01 DE 05137-01)

An acid etch, resin technique has been proposed for conservatively restoring cervical erosion lesions. Little is known about the micromorphologic features of these lesions as they affect dentin and pulp. The objective will be to determine the histologic features of: 1) surface of the lesion, 2) changes within the dentin, 3) the type of reparative dentin, and 4) pulp changes. In addition, the morphologic features of acid conditioned, eroded dentin and its appearance after placement of N-phenyl glycine-glycidyl methacrylate (NPG-GMA) will be determined along with the physical relationship between such treated surfaces and composite resin. The determinations will be made using light and scanning electron microscopy and contact microradiography.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $31,389

9.0023, DESIGN AND DEVELOPMENT OF IMPROVED COMPOSITES

W.E. Brown, American Dental Assn., Health Foundation, Research Unit, *211 E. Chicago Ave., Chicago, Illinois* 60611 (R13 DE 04936-01)

A one-day symposium to advance the science of dental composites is to be held to mark the 50th anniversary of the American Dental Association's participation in research at the National Bureau of Standards. The principal objective of the symposium, entitled 'Design and Development of Improved

Composites', is to accelerate the incorporation of known improvements into commercial composites and to identify the directions for future improvements in the ingredients and properties. This symposium is to be directed primarily to dental materials researchers, teachers and manufacturers, and is to be held in conjunction with the IADR-AADR meeting in Washington, D.C. March 16 -19, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

9.0024, REPLICA-SEM STUDIES OF IN VIVO DENTAL MORPHOLOGIES

G.W. Marshall, Northwestern University, Chicago Campus, School of Dentistry, Dept. of Biological Materials, *Chicago, Illinois* 60611 (R23 DE 04000-03)

A replicating technique for teeth and restorations was developed and evaluated over the past project period. The technique utilizes a polyether impression which is cast into epoxy positive replicas for SEM evaluation. The technique has been used to reproduce etched enamel in clinical patients and to show changes in amalgam restorations placed in dogs with excellent duplication of the subject. These techniques will be applied to the study of time-dependent morphological changes of etched enamel, amalgam restorations, composite restorations, evaluation of orthodontic bracketing procedures, and plaque accumulation. All studies will be conducted on clinical patients.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

9.0025, EVALUATION OF NEW FILLERS FOR DENTAL COMPOSITE RESINS

H.D. Moskowitz, College of Medicine & Dentistry of New Jersey, New Jersey Dental School, School of Dentistry, Dept. of Dental Biomaterials, *100 Bergen St., Newark, New Jersey* 07103 (R23 DE 04334-03)

Evaluation of two new types of fillers for restorative composite resins is being conducted. One type of filler is a porous silica glass intended for anterior restorations where improved polishability is desired. The other is a porous surface nickel powder. This powder is intended to improve the wear resistance of posterior composite systems.

Four experimental fully loaded silane treated porous composites have been prepared from two different BIS-GMA monomer formulations and two different pore size glasses. BIS-GMA monomers were prepared to give a wide viscosity range. One porous glass filler had an average pore diameter of 2000 angstroms and the other had an average of 40 angstroms. The large pore filler was added as a single particle size and the maximum loading achieved was 41% by weight. The fine pore powder was added in a continuous size distribution and had a maximum loading of 54%.

Solvent extraction techniques were used to determine the amount of residual monomer contained in the cure samples. The large pore filler lost an average of 1% and the fine pore material lost an average of 0.8% by weight. Large pore samples had a one day compressive strength of 21000psi and the fine pore systems have an average of 25000psi.

The large pore samples had a coefficient of thermal expansion of 58 ppm and the fine pore system had a coefficient of 45 ppm.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$41,150

9.0026, X-RAY AND SEM ANALYSIS OF CU RICH DENTAL AMALGAM

S.J. Marshall, Northwestern University, Chicago Campus, School of Dentistry, Dept. of Biological Materials, *Chicago, Illinois* 60611 (R23 DE 04704-03)

This project is designed to study two particular aspects of copper rich dental amalgams. The microstructures of 13 commercial systems have been qualitatively compared with each other and with a conventional amalgam system. The major difference is the replacement of most of the weak, corrosion prone gamma 2 (Sn-Hg) phase with Cu6 Sn5. The initial formation of the gamma 2 phase and its subsequent disappearance and the relative growth of the Cu6 Sn5 phase have been studied by X-ray diffraction. An attempt will be made to determine the quantities of each phase present as a function of time. Major corrosion products on conventional amalgams have been identified as Sn4(OH)6Cl2 and SnO. Products are being grown in chloride and sulfide solutions on the copper rich amalgams and will be compared with those from the conventional amalgams. This comparison is done by scanning electron microscopy, energy dispersive X-ray analyses, and X-ray diffraction for morphology, chemical composition and comparison with d-spacings of known compounds.

BIBLIOGRAPHIC REFERENCES: Marshall, S. J. and Marshall, G. W.: Identification of Corrosion Products in Dental Amalgams. Accepted for the 1979 Int. Biomaterials Symposium, Clemson, S.C., April 28 - May 1, 1979. Marshall, S. J. and Marshall, G. W.: Aging vs. Relative Quantities of Amalgam Phases. Accepted for the 55th General Session AADR/IADR, New Orleans, La., March 29 - April 1, 1979.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $22,539

9.0027, WEAR OF DENTAL RESTORATIVE MATERIALS

W.F. Bailey, University of Connecticut, Storrs Campus, School of Liberal Arts & Sciences, Dept. of Chemistry, *Storrs, Connecticut* 06268 (R23 DE 04708-03)

The proposed research is designed to aid in the development of dental filling materials with improved wear resistance through systematic investigation of the fundamental processes responsible for physiological wear.

The objective is pursued in two complimentary ways using recently developed instrumentation designed to test for pure sliding wear and for pure normal or compound impact wear. The two novel wear-testing instruments were designed and constructed at the University of Connecticut and are unique in their capabilities, controllability and applicability to studies of wear of dental restorative materials. Using our laboratory system dental filling materials can be subjected to stress histories which replicate those experienced in vivo. This will allow for the rapid determination of the resistance of various dental filling materials to wear against carefully prepared sections of human tooth before they are subjected to time-consuming, extensive clinical evaluation.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $15,050

9.0028, PHYSICOCHEMICAL MODIFICATIONS OF DENTAL RESTORATIVES

S.I. Stupp, Northwestern University, Chicago Campus, School of Dentistry, Dept. of Biological Materials, *Chicago, Illinois* 60611 (R23 DE 05152-01)

The present research program will explore the possibility of enhancing, simultaneously, adhesion and wear resistance in polymeric restoratives through the action of electrostatic forces. This approach is, in part, based on preliminary experiments and other previous investigations which suggest the existence of electrostatic potentials on tooth surfaces. Electrostatic potentials will be incorporated in various components of restorative materials (fillers, polymeric powders and in situ polymerized matrices) as a means to promote adhesion at both tooth/restorative and filler/matrix interfaces. Their incorporation will be carried out by a combination of thermoelectric pre-treatments and minor chemical modifications of acrylic resins. These modifications will involve copolymerization of small amounts of ionizable monomers (methacrylate salts) with conventional acrylic compounds. Conventional procedures will be used to characterize mechanical properties of formulated restoratives such as hardness, tensile and compressive strengths. Any changes in glass transition temperatures and/or development of structural order due to polymerization in the presence of electrostatic fields will be assessed by differential scanning calorimetry and X-ray diffraction techniques. Marginal adaptation and adhesion to both enamel and dentin surfaces will involve scanning electron microscopy and in vitro mechanical tests, respectively. An infrared spectroscopic technique has been proposed as a means to evaluate in vitro wear resistance of the various restorative formulations.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $34,490

9.0029, DENTAL ALLOY CORROSION RESEARCH

T.K. Vaidyanathan, New York University, School of Dentistry, Dept. of Dental Materials Science, *421 1st Ave., New York, New York* 10010 (R23 DE 05314-01)

This proposal seeks to establish the correlation between the corrosion and tarnish properties of low precious metal dental casting and porcelain alloys with the chemical composition and microstructures of the alloys. In addition the influence of new alloying elements such as Pd, In and Ti on dental amalgam compositions will be studied. Anodic potentiostatic polarization, alternate immersion tarnish characterization, microstructural studies and mechanical properties characterization will be utilized in establishing the correlation. An organized analysis of the the relationships between the chemical composition and microstructures with the corrosion properties must begin at binary systems and proceed to more complex multicomponent alloys. Such a study would be extremely beneficial because such data could be utilized in the proper selection of dental casting alloys by the clinicians and for the proper design of alloy compositions by the manufacturers. In addition, from a scientific point of view, such a study is long overdue.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$31,250

9.0030, CLINICAL EVALUATION OF ANTERIOR AND POSTERIOR DENTAL RESTORATIVE MATERIALS

J.P. Moffa, U.S. Dept. of Health & Human Services, Public Health Service, Hospital, *15th Ave. & Lake St., San Francisco, California* 94118 (Y01DE50019 (CONTRACT))

OBJECTIVES AND WORK SCOPE: The offeror proposes a long-term clinical study designed to evaluate three types of currently used dental restorative materials: (A) base metal alloys for use in fixed prosthodontics: (1) a beryllium-containing base metal alloy, (2) a non-beryllium-containing base metal alloy, and (3) a control conventional gold, platinum, palladium alloy. Additional aims of this study will involve the determination of the physical and mechanical properties of the three alloys. (B) Three dental amalgam alloys which possess low creep properties: (1) two experimental single phase alloys, and (2) a control dispersed phase alloy. Additional aims of this study will involve the determination of the mechanical properties of the three alloys. (C) A composite resin used as a restorative material in posterior teeth. Additional aims of this study will involve an assessment of the mechanical properties of the resin with particular emphasis on the development of an in vitro wear test that would be predictive of the resin's clinical wear characteristics.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$136,659

9.0031, DISCONTINUOUS GAMM-2 PHASE AND MARGINAL FRACTURE IN AMALGAM

J.D. Preston, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-008-P)

Approximately 20 amalgam fillings have been placed in one patient only. Obtaining type of patient necessary for this study has been difficult. We wish to continue this study and anticipate study results to be slow over the next two years because of the difficulty in finding patients who fit the criteria.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

9.0032, CLINICAL EVALUATION OF CERVIDENT - A CLASS V RESTORATIVE

M.H. Reisbick, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *San Antonio, Texas* 78284 (671-001-F)

Treatment of tooth surfaces with various acids and polymers to promote adherence of resins has received widespread attention. Previous attempts to restore Class V erosion type lesions, without mechanical preparation, has been unsuccessful. Recently, two new systems, Cervident and Aspa, have been introduced. The purpose of this study was to clinically evaluate these systems. Because of less desirable features, Aspa, was evaluted on a limited basis. One hundred lesions were selected from patients under treatment at either Audie Murphy V.A. or Mckown Dental Clinic in San Antonio. Eighty lesions were treated with Cervident while 20 were treated with Aspa. To date, evaluations have been made by three investigators at baseline, 6, 12 and 18 months. Those receiving treatment at Audie Murphy were evaluated using the Ryge method, while both the Ryge and Chandler methods were used at McKown. The purpose was to compare the two methods of evaluation since certain shortcomings seem to exist singly.

Essentially, the results for Audie Murphy and McKown indicate 73% and 76% retention after one year for Cervident - Aspa showed 66% retention. Color match was initially poor and remaind essentially the same for Aspa; color match was good for Cervident. Tooth sensitivity, due to pretreatments, was not noticed. Each system of evaluation holds certain advantages but good agreement is difficult with the Chandler method. Very small or saucer-shaped lesions, predominantly in enamel, appear to be contraindicated for this type of restoration; perhaps better case selection would improve the retention statistic.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

9.0033, THE INFLUENCE UPON STRENGTH OF VARIOUS MATERIALS INCORPORATED IN ETCHED COMPOSITE RESIN BRIDGE

E.J. Sweeney, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Leavenworth, Kansas* 66048 (686-001-F)

The acid etched bridge technique was tested on extracted teeth on an Instron testing machine along with three variations of it.

The three variables tested were: (1) Class III preparation; (2) Class III preparation plus arch wire; (3) Fiberglass.

The greatest strength was shown by Group 1, followed by the norm and Group 2, then Group C.

The fracture of the norm occurred thru the union of the filled and unfilled resin.

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U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

9.0034, CORROSION AND DISCOLORATION IN AMALGAM

J.J. Cuello, Universidad Nacional de Cordoba, Facultad de Odontologia, Catedra de Clinica de Operatoria Dental, *5000 Cordoba, Argentina*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY
(No Supporting Organization
Reported) funds n.a.

9.0035, PROTECTION AND ISOLATION FACTORS IN THE USE OF MATERIALS FOR TEMPORARY RESTORATIONS

J.J. Cuello, Universidad Nacional de Cordoba, Facultad de Odontologia, Catedra de Clinica de Operatoria Dental, *5000 Cordoba, Argentina*

No summary has been provided to the Smithsonian Science Information Exchange.

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Reported) funds n.a.

9.0036, ALTERATIONS IN CAVITY LINING MATERIAL BY COMPRESSION FORCES

E.J. Uribe, Universidad Nacional de Cordoba, Facultad de Odontologia, Catedra de Tecnica de Operatoria Dental, *5000 Cordoba, Argentina*

Clinical findings in a high percentage of cases indicate that the marginal fractures which occur are due to the plastic deformation of the base material in contact with the proximo-occlusional amalgam.

Resistance to condensation and compression forces was studied at 30 minutes, one hour, 24 hours and one week immediately following addition of amalgam to base.

Structural and surface alterations of the pulp insulators calcium hydroxide (Dycal), zinc oxide-eugenol; zinc-oxide-eugenal with zinc acetate, IRM, and zinc phosphate cement were studied by subjecting them to filling pressure, with silver amalgam, both mechanically and manually for 3 minutes.

Surface alterations were micrometrically measured with a photo microscope. Dental materials were cut longitudinally, medio-occlusional cavities were etched and then sealed using a special instrument which avoided distortions of the base surface. (Translated)

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Reported) funds n.a.

DIAGNOSIS & TREATMENT - BONDING AGENTS

9.0037, FEASIBILITY STUDY AND DEVELOPMENT- AN ADHESIVE TO DENTIN AND TOOTH ENAMEL

M. Dichter, Polymer Corp. of America, *2186 Mill Ave., Brooklyn, New York* 11234 (DAMD17 78 C 8076)

Although there is an urgent military requirement for a true dental adhesive, to date, no effective and biocompatible adhesive has been found. The ability of a polymer to chemically bond with tooth structure would provide a revolutionary treatment modality for maxillofacial injuries. This type effort also has the potential of revolutionizing some of the restorative phases of dentistry.

Suitable catalysts, graft initiators, promoters, and solvents will be involved in the grafting process. Standard grafting procedures will be used, initially, with process parameters being developed and modified as the study progresses in order to achieve the most effective process. samples will be simultaneously evaluated by the USAIDR for adhesive strengths.

SUPPORTED BY
U.S. Dept. of Defense, Army,
Medical Research &
Development Command, Inst.
of Dental Research $49,335

9.0038, CHARACTERIZATION OF ADHESIVE FORMED BY MYTILUS EDULIS

D.P. DeVore, Battelle Memorial Inst., Biomedical Sciences Section, *505 King Ave., Columbus, Ohio* 43201 (R01 DE 04100-03)

Adhesive disc precursor secretions will be collected from the distal depression of the foot of the sea mussel Mytilus edulis after chemically stimulating the secretory process. Secretions will be stored in NaCN or acetylimidazole to prevent hardening. Protein components of the secretions will be isolated and purified using column chromatography and polyacrylamide disc gel electrophoresis. Particular emphasis will be placed on characterizing the enzymic component of the adhesive. Experiments to obtain adhesive disc precursors from isolated secretory vesicles will also be initiated. Research will be continued to study the mechanism of the hardening process by following the formation of tyrosine cross-links in chemically and enzymically treated precursor secretions and in similarly treated precursor secretion fractions and fraction combinations. Finally, it is expected that preliminary experiments will be conducted to demonstrate in vitro formation of hardened adhesive material from precursor secretions. Results from these experiments could ultimately lead to the application of the secretion as a hard tissue adhesive.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

9.0039, BLOCKED ISOCYANATES FOR CHEMICAL BONDING TO DENTIN

W.H. Snyder, New Jersey Inst. of Technology, School of Engineering, Dept. of Chemial Engineering & Chemistry, *323 High St., Newark, New Jersey* 07102 (R01 DE 05053-01)

The proposed research will concentrate on the following objectives and methods: (a) Synthesis, purification and characterization of blocked isocyanate functions of 2, 4-tolylenediisocyanate (TDI), the mono adducts of TDI with hydroxyethyl methacrylate (HEMA) and TDI adducts of HEMA-methyl methacrylate (MMA) copolymers. (b) Study of the interaction of these blocked isocyanate functional adducts with dentin and enamel using attenuated total reflectance (ATR) in the infrared and scanning electron microscopy (SEM). (c) Formulation of selected blocked isocyanate functional materials into fast-setting adhesive systems. (d) Investigation of adhesion to dentin and enamel by destructive methods (shear and tensile tests) and examination of the mode of failure by SEM. (e) Measure tensile strengths, shear strengths and glass transition temperatures by known methods. Differential thermal analysis will be used to estimate glass transition temperatures.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$59,288

9.0040, ASSESSMENT OF WEAR OF FOUR DIFFERENT SEALANTS IN VIVO

O.E. Jensen, Eastman Dental Center, Dept. of General Dentistry, *800 Main St. E., Rochester, New York* 14603 (R23 DE 05042-01)

This study will determine differences in wear characteristics between self polymerizing and ultraviolet light polymerizing sealants, and between unfilled and filled sealants. The teeth used in the study will be unrestored, caries-free second molars and second bicuspids. A total of 60 subjects will be sealed initially, with one sealant type used in all four quadrants. Quantitative measurements will be obtained using silver copings made from immediate post-sealant tooth replica models. The amount of sealant applied will be determined by placing the pre-sealant die into immediate post sealant coping. A silicone-base impression material will be placed in the copings immediately prior to the placement of the dies, and a reproducible force will be applied on the die and coping. The volume of the sealant present will be calculated from the weight of the impression material between the die and the immediate pot-sealant coping using a micro-balance. At 1, 6, 12, and 24 month recall visits, full arch impressions will be taken and tooth replica models will be made. Post-sealant recall dies will be placed in the silver copings and sealant loss will be determined using the same procedure. Sealant loss will be reported as a percentage reduction in the volume initially applied to the occlusal surfaces. The data will be statistically evaluated by performing an analysis of variance with repeated measures in time. Scanning electron micrography will be done on a limited number of teeth after two years. Three teeth will be selected from each of the four treatment groups, and from each of three retention levels, sealant intact, sealant partially lost, and sealant clinically undetectable, for a total of 36 teeth. Profile changes will be assessed by sectioning the silver copings with the tooth replica models in place. Each half will be photographed on B/W sheet film, and tracings of the photographs from each half will be superimposed to give a picture of the wear profile throughout the two year study period.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$28,215

9.0041, INTERACTIONS OF ORAL STRUCTURES & RESTORATIVE MATERIALS

J.M. Cassel, U.S. Dept. of Commerce, National Bureau of Standards, *Washington, District of Columbia* 20228 (Y01DE40015 (CONTRACT))

OBJECTIVES AND WORK SCOPE: The study is being performed to obtain new knowledge on the properties and interactions of oral structures and restorative materials. The subject matter to be explored and studied, including subtasks, is as follows: 1. Adhesion of Restorative and Caries-Preventive Materials to Tooth Surfaces: A. Surface Characterization of Dental Materials by Water Adsorption. B. Novel Approach to Development and Assessment of Adhesion in Dental Materials. C. Synthesis for Improvement Adhesion and Stability of Composite Restorative and Sealant Materials. D. Polymer Grafting, A Technique for Bonding to Mineralized Collagen Surfaces. 2. Physical, Mechanical and Physicochemical Properties of Hard and Soft Tissues of Dental Materials: A. Dimensional Changes in Tooth Structure. B. Wear Resistance of Dental Restorative Materials. C. Zinc-Polycarboxylate Dental Cement, Properties, and Technique for Improvement.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$426,000

9.0042, CLINICAL EVALUATION OF DENTAL CEMENT SOLUBILITY ON DENTURE PATIENTS

D.G. Gronas, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Vancouver, Washington* 98661 (683-001-P)

Five different classes of dental luting cements have been tested in denture wearing patients for six month periods to check the solubility in the oral environment. Enclosed is a reprint of the article giving details of some of the results of the research through last year. We are presently doing further evaluation of four cements that have been in for six months in thirteen patients.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

9.0043, STUDIES ON POLYMER REINFORCED ZINC OXIDE-EUGENOL CEMENTS

R.L. Macchi, Universidad de Buenos Aires, Facultad de Medicina, Dept. of Dental Materials, *Velez Sarsfield 405, Buenos Aires, Argentina* (6235)

The objective of the project is to develop low-cost intermediate restorative cements to be used in public health programs. Commercially available zinc oxide-eugenol cements were 'in vitro' and clinically tested to establish the general properties of this type of products.

The use of different reinforcing agents was then assessed and organic polymers were finally selected as the most efficient way of improving the behavior of the materials. Different acrylic, vinylic and other types of polymers were used and several of them proved to be a satisfactory.

The structure of the composite formulas was studied under scanning electron microscopy and general parameters on which the reinforcing effect is obtained have been established.

Different mechanical properties were evaluated in the most promising formulations and they were correlated with the results obtained in different wear and friction studies. Their long term stability was evaluated by determining their sorption, solubility and mechanical properties after up to a 4-month immersion in artificial saliva at pH 6.7.

Clinical evaluation of these formulations is now being carried out in young patients.

SUPPORTED BY

Consejo Nacional de Investigaciones Cientificas y Technicas	$30,000

9.0044, THE FROZEN-SLAB-TECHNIQUE IN SETTING OF DENTAL CEMENTS

B. Rossiwall, Freie Universitat Berlin, Inst. fur Klinisch Theoretische Zahn Mund & Kieferheilkunde, *Assmannshauserstrasse 4-6, 1000 Berlin 33, Federal Republic of Germany*

The frozen-slab-technique - a mixing procedure for cementing orthodontic bands - has been found to increase the working time and decrease the setting time of dental cements. Factors controlling the hardening of cements are explained by material tests as well as by electron microscopic investigations of the internal texture.

SUPPORTED BY

Freie Universitat Berlin	funds n.a.

DIAGNOSIS & TREATMENT - PROSTHESES - FACIAL

9.0045, COMPOSITE MATERIALS FOR MAXILLOFACIAL PROSTHESES

R.A. Erb, Franklin Inst. of the State of Pennsylvania, Research Lab, *20th & Benjamin Franklin Pkwy., Philadelphia, Pennsylvania* 19103 (DAMD17 77 C 7059)

Develop a materials system which will be: (1) capable of being easily and inexpensively fabricated to various human facial shapes and forms and to various human racial colors and tones, (2) capable of withstanding the stresses of environmental sunlight, temperature, and humidity without deterioration to the material's flexibility and color for a minimum of two years, (3) capable of being easily cleansed by soap and water if solid via factors normally encountered in day-to-day activities, (4) compatible with surgical appliance cements and similar skin adhesives, and (5) applicable for clinical use and potentially acceptable to clinical use and potentially acceptable to clinicians active in the area of rehabilitation.

A system will be designed which will be suitable for microencapsule-making experiments with the concentric flow technique. from this will be selected a number of promising castable elastomeric materials for participation in the investigations. On various developed composites, measurements will be made on basic mechanical properties in tension and compression. The final step will be a cooperative effort between the F.I.R.L. And the sponsor for animal/human evaluations.

SUPPORTED BY
U.S. Dept. of Defense, Army,
Medical Research &
Development Command,
Medical Bioengineering
Research & Development Lab. $56,195

9.0046, DEVELOPMENT OF MATERIALS FOR MAXILLOFACIAL PROSTHESIS

D.R. Cowsar, Southern Research Inst., *2000 9th Ave. S., Birmingham, Alabama* 35205 (N01DE42435 (CONTRACT))

OBJECTIVE: Complete developmental phase by determining stain resistance, wettability, cleanability, dimensional stability, opacity, and adhesion to tape and surgical adhesive; optimizing bulk viscosity, pot life, vulcanization time and temperature, mold release and shrinkage, and intrinsic and extrinsic coloration techniques; evaluating special techniques for fabricating hollow, foam-filled, or microballoon-filled prostheses. Conduct pre-clinical phase by formulation of larger batches, determination of storage stability, and evaluation with animals of the dermal and ocular toxicity of the components of kits and the cured silphenylene elastomers. Conduct clinical phase by fabrication of custom prostheses for patients and follow-up by inspection, interview, and examination of patients and questionnaire of patient acceptance, wear characteristics, and shortcoming of the silphenylene prostheses.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

9.0047, MAXILLOFACIAL MATERIALS

F. Leonard, George Washington University, School of Medicine & Health Sciences, Dept. of Medicine, *2121 Eye St. N.W., Washington, District of Columbia* 20037 (R01 DE 03860-06)

In this project we are investigating the synthesis crosslinking and compounding of latex dispersed acrylic acid ester elastomers for use in casting extraoral maxillofacial prostheses. The films prepared are tested for room temperature mechanical properties, low temperature flexibility strain and ultraviolet light resistance. Dermotological test to determine skin reaction are carried out on promising elastomers. Maxillofacial prostheses such as ears and noses are prepared from the latices and efforts will be undertaken to transfer the technology to laboratories interested in preparing improved prostheses.

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Services, Public Health Service,
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National Inst. of Dental
Research $61,415

9.0048, MAXILLOFACIAL MATERIALS--COLOR STUDY

A. Koran, University of Michigan, Ann Arbor Campus, School of Dentistry, Dept. of Dental Materials, *Ann Arbor, Michigan* 48104 (R01 DE 04136-05)

Maxillofacial appliances fail clinically for two reasons: (1) color instability of the pigmented material, and (2) degradation of the static and dynamic physical properties. Several maxillofacial materials have demonstrated excellent color stability when exposed to accelerated aging. However, when these same materials were pigmented with available maxillofacial pigments some pigments were color stable while others were not. Many of these pigments were also toxic in tissue culture tests. It is the purpose of this study to evaluate intensely colored ceramic powders as maxillofacial pigments since they are most likely color stable and non-toxic. These materials also have potential for chemical treatment which would create a chemical bond between the elastomers and the ceramic pigments. Other pigment systems will be evaluated also. Specifically, the most color stable maxillofacial materials will be pigmented with: (1) individual pigments and then (2) combinations of pigments to match chosen skin tones. New types of maxillofacial materials will be added to the study when they become available. The samples would then be subjected to: (1) static and dynamic physical testing, (2) spectrophotometric analysis to measure color, and (3) toxicity testing. The samples would then be placed in a weathering chamber for 900 hours after which the testing sequence would be repeated. The results of this study will determine: (1) which pigments are color stable when combined with the various elastomers, (2) which combinations produce the most favorable static and dynamic physical properties, and (3) which combinations are non-toxic. The results of this study will have great impact upon the field of maxillofacial prosthetics by significantly extending the life expectancy of maxillofacial prostheses.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $96,989

9.0049, RESEARCH OF POLYURETHANES FOR MAXILLOFACIAL USE

T.E. Fischer, University of Alabama in Birmingham, School of Dentistry, Dept. of Biomaterials, *1919 7th Ave. S., Birmingham, Alabama* 35233 (R01 DE 04138-05)

The object of this program is to develop and evaluate polyurethane elastomers for use as maxillofacial prostheses. Several commercially-available materials were tested and compared with materials currently being used for prostheses, and two promising systems were identified. One is a two-component commercially-available system, Calthane ND2300. Part A is an aliphatic diisocyanate-terminated prepolymer and Part B is a hydroxy-terminated polyester. The two components when mixed together with suitable antioxidants and UV stabilizers react to form an elastomer that has potential as a prosthetic material. The other system is a new polyurethane involving several commercially-available components. Isophorone, an aliphatic diisocyanate, and Polymeg, an aliphatic polyether diol, are combined to form a reactive prepolymer. This liquid prepolymer is converted to an elastomer by combining it with 1,4-butanediol as a chain extender, and 1,2,6-hexanetriol as a cross-linking agent. This aliphatic polyurethane exhibits exceptional mechanical properties. Properties such as tensile strength, hardness, modulus, and tear strength can be optimized by adjustment in the ratio of isocyanate to hydroxyl groups in the formulation. The addition of UV stabilizers has resulted in a polymer that retains most of its mechanical strength even after many hours of accelerated aging tests. Although clinical tests have not yet been performed, these two systems show promise as future maxillofacial materials.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $67,951

9.0050, CHLORINATED POLYETHYLENE FOR MAXILLOFACIAL PROSTHESES

P.D. May, Lake Pontchartrain Lab., Membrane Technology, *5010 Camp Leroy Johnson Dr., New Orleans, Louisiana* 70126 (R01 DE 04392-03)

Maxillofacial prostheses are being prepared from polymer alloys consisting mainly of chlorinated polyethylene. Indications are that this material is superior to existing elastomers used for this application; only simple equipment and essentially untrained personnel are required to form the prostheses. Actual clinical testing has been carried out in the second year of the project with 13 patients. These clinical studies will be continued and expanded in the final year. Detailed performance descriptions, including color and dimensional stability measurements, will be obtained. Strain resistance and general appearance in vivo will be closely evaluated. Animal testing will be continued to verify the safety and non-irritating nature of the polymer. Outdoor weathering tests are being extended to provide a more definitive indication of long-term performance. Surface treatments of the protheses are being investigated to enhance life-like appearance over longer periods of actual wear.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

9.0051, DEVELOPMENT OF SAFE AND ADEQUATE ADHESIVES FOR MAXILLOFACIAL CONSTRUCTS

J.F. Lontz, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Maxillofacial Research Lab, *1601 Kirkwood Hwy., Wilmington, Delaware* 19805 (460-002-P)

The attachment of external orofacial prosthesis for disfigurement requires use of non-inflammatory and otherwise harmless adhesive formulations. It has now been established that polyisobutylene (PIB), compared to low molecular weight latices of polymethylmethacrylate (Acryloids) and polyurethanes are less inhibitive and less toxic, to tissue and tissue growth using human excised donor (HED) tissue culture, a testing procedure now being used for demonstrating safety for medical devices. A series of PIB formulations are being prepared using chamois as the collagen adherand in its dry and reconstituted form to replicate the physiological hydrophyllic (sweat constituents) and hydrophobic (lipid constituents, notably glyceride) conditions. While adequate adherence of the PIB formulations to the collagen (chamois) ssbtrates is achieved, the corresponding adherence to the prosthesis surface is usually only a fraction of the adhesion stress to the collagen and needs to be significantly increased. The program now involves continued modifications of the PIB formulation to enhance the adhesion to the prosthesis substrate in a test procedure being devised for practical relevance.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

9.0052, DEVELOPMENTS OF NEW ELASTOMERIC PROSTHETIC MATERIALS

M. Braden, University of London, London Hospital Medical College, Dept. of Materials Science in Dentistry, *Turner St., London E1 2AD, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$10,028

DIAGNOSIS & TREATMENT - PROSTHESES - ORAL

9.0053, RESPONSE OF COMBINED ELECTRICAL STIMULATION AND BIODEGRADABLE CERAMICS

J.E. Lemons, University of Alabama in Birmingham, School of Dentistry, Dept. of Anatomy, *1919 7th Ave. S., Birmingham, Alabama* 35233 (DAMD17 75 C 5044)

Latest combat figures indicate a 12 percent incidence of maxillofacial injuries. Of these, 55 percent are avulsive wounds of the mandible which require extensive and time consuming, surgical procedures. In addition, the soldier is lost from combat and support duty for multiple extended periods of time while immobilization and grafting operations are performed. Psychological problems and length of convalescence are directly attributable to the soldier's ability to function normally and accept nutrition. The objective of this study is to demonstrate the feasibility of using an alloplastic grafting material (biodegradable tricalcium phosphate ceramic) enhanced by electrical stimulation at appropriate healing periods to synergistically achieve new bone growth, more rapidly, and therefore eliminate problems associated with current surgical techniques.

This study is a complementary effort to other biodegradable ceramic investigations supported by this office. Currently investigations address the material's characterization, in vitro effect, and new physical forms to support other newly identified applications. Other studies are developing simple methods of bone grafting for use in periodontal and oral surgery procedures. This new effort would be another enhancing application making this a comprehensive and complete research study. The approach of this effort would be- (1) to develop and evaluate an animal model for studying the combined techniques of applying direct electrical stimulation to tissue ingrowth and stabilization of a porous biodegradable ceramic- (2) to evaluate the kinetics and tissue response to the ceramic in surgical lesions- and (3) to evaluate the kinetics responses of combined electrical stimulation and ceramic with the same animal system.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research	$48,328

9.0054, AUTOMATED CROWN REPLICATION USING SOLID PHOTOGRAPHY

R. Schmidt, Solid Photography Inc., *Melville, New York* 11746 (DAMD17 78 C 8055)

Objective of project is to reproduce dental crowns and other suitable appliances without the time-consuming and expensive methods currently in use. The successful pursuit of this project would reduce time presently spent in numerous technical procedures by professional personnel and permit more rapid return of personnel to unit/duty. further pursuit of this project would explore the feasibility of exact replication of hard structures prior to surgery to correct avulsive wounds.

The general procedure will be to use the 3-d process micro studio to obtain the three dimensional surface information from a wax pattern of a crown. This information will be stored on a computer tape and used to automatically control a numerically controlled milling machine to carve a finished crown directly from metal without conventional mold and casting procedures.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research	$59,890

9.0055, DEVELOPMENT AND EVALUATION OF NITINOL FOR USE IN DENTISTRY

E.F. Huget, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Dental Materials, *Washington, District of Columbia* 20314 (DA0D6048)

To exploit the shape memory phenomenon of 55-nitinol for enhancement of the treatemtn capabilities of the Army dentist and physician. Realization of the conceptual uses of this unusual metal will result in substantial savings of laboratory costs and professional man-hours.

To design, fabricate, and test by means of animal and human studies, the following devices- (1) flexible wire clasps that will withstand accidental deformation out of the mouth, yet recover in the mouth- (2) prestressed surgical fixation staples and plates that will bend or contract slightly at body temperature, bringing bone fragments into close approximation or under slight compression- (3) self-anchoring fixation pins and endosseous implant devices- (4) collapsible devices for placement into defects (cyst cavity, cleft palate, etc) through orifices smaller than the inside diameter- (5) fixed and removable prosthetic appliances, restorations or precision attachments that can move into undercuts in the mouth.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research	funds n.a.

9.0056, PROSTHETIC REHABILITATION OF OROPHARYNGEAL CANCER

J.A. Logemann, Northwestern University, Chicago Campus, School of Medicine, Dept. of Otolaryngology & Maxillofacial Surgery, *303 E. Chicago Ave., Chicago, Illinois* 60611 (R18 CA 20876-03)

This study is designed to evaluate the effects of an intra-oral prosthesis on the communication and nutritional rehabilitation of patients, following ablative oral surgery for cancer. The ultimate goal is to develop an inexpensive, simply designed prosthesis which can facilitate rapid rehabilitation of this group of patients. Prostheses will be designed and constructed for 45 patients, 9 patients in each of the following surgical categories: 1) anterior floor of the mouth; 2) composite resection including hemimandibulectomy and excision of a portion of the palate and posterior tongue; 3) composite resection including hemimandibulectomy and excision of less than 60% of the tongue; 4) composite resection including hemimandibulectomy and excision of more than 60% of the tongue; 5) extended supraglottic laryngectomies including base of the tongue. Prior to construction of the prosthesis, each patient's vocal tract function is evaluated, including detailed studies of oral, pharyngeal and esophageal function during swallowing and oral and pharyngeal function during speech. These data are used as the basis for construction of the prosthesis. After the prosthesis is completed, each patient's function is re-evaluated. If necessary, changes are made in the design of the prosthesis to further optimize function. A final functional evaluation is made after completion of the prosthesis. Each patient serves as his own control. The pre- and post-prosthetic functional patterns are compared to provide an objective picture of the effects of the prosthesis on the patient's day-to-day functions. Results of the evaluations will be compared within each patient group; comparisons between groups will also be made.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$63,890

9.0057, CORROSION OF PRECIOUS METAL ALLOYS

K.F. Leinfelder, University of North Carolina, Chapel Hill Campus, School of Dentistry, *Chapel Hill, North Carolina* 27514 (R01 DE 04101-05)

A combined laboratory-clinical investigation is proposed to evaluate the performance of commercial low-gold, and gold substitute dental casting alloys. Nine commercial alloys of this type will be evaluated including low-gold gold-base alloys, silver-palladium and nickel-chromium alloys. In addition, seven experimental formulations of related composition will be studied. The laboratory study will evaluate the composition, microstructure hardness, tensile properties, heat treatability, corrosion resistance, fit and burnishability of castings of these materials. Clinical inlay castings will be prepared to evaluate intra-oral fit, burnishability, tarnish and corrosion, wear and marginal integrity. The research of the laboratory and clinical evaluations will be correlated to select the best (most predictive) in vitro corrosion test. Correlations will also be sought between various properties and structural characteristics of the alloys and clinical performance as a basis for selecting improved materials.

BIBLIOGRAPHIC REFERENCES: Sturdevant, C.M., Leinfelder, Karl F., and Kusy, Robert F., Clinical and Laboratory Evaluation of Low Gold Alloys, I.A.D.R. Abstract No. 415, March, 1979.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $73,140

9.0058, BONDING OF PORCELAIN TO SEMI- AND NON-PRECIOUS METALS

C.W. Fairhurst, Medical College of Georgia, School of Dentistry, Dept. of Dental Materials, *1459 Gwinnett St., Augusta, Georgia* 30902 (R01 DE 04252-05)

The aims of this project were to study bonding of porcelain to metal systems used in dentistry: specifically, the bonding mechanism, the effect of coefficient of contraction (alpha) of metal and porcelain on interfacial shear stress and the effect of casting variables on the metal used in these systems. The new scanning electron microscope and new laboratory facilities have recently been installed and will be of significant value in these studies in the years to come. Experimental programs have proceeded in this first year to fulfill the objectives. Thermal contraction data on fourteen alloys and six porcelains have been gathered. New mathematical treatments of these data have been developed to better approximate the effect of an interfacial shear stress. New thermal shock bond tests are being developed which should lead to a better understnading of the correlations, if any, of the alpha value and bonding. Softening temperatures of the opaque and body porcelains have been determined. These data are of significance in evaluating the compatibility of the metal-porcelain system. Also high temperature creep values of the metals have been determined to better evaluate the differences between precious and nonprecious alloys in their clinical distortion characteristics.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $90,264

9.0059, IMPROVED LUMINOPHORS FOR DENTAL PORCELAIN

W.T. Wozniak, American Dental Assn., Health Foundation, Division of Biophysics, *211 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 04709-02)

A large majority of the commercially available dental porcelains contain uranium, a radioactive element. The uranium is present in dental porcelain in order to simulate natural tooth fluorescence. Recent studies indicate that the radiation dose to the oral mucosa from the uranium in dental porcelain may be excessive.

The objective of this investigation is to seek suitable non-radioactive luminophors for incorporation into dental porcelain which simulate natural tooth fluorescence and which can withstand the high temperatures necessary for fusing and firing the ceramics. All luminescing materials will be observed with respect to their emission characteristics in a spectrofluorometer modified so that correlated spectra can be obtained.

After compounds are found that have a similar fluorescence to natural teeth, they will be used to construct representative porcelain specimens. These specimens will be prepared from porcelain base material and fired in the usual manner for making porcelain teeth. The fluorescence spectra of the porcelain specimens will then be obtained and compared with the results for the agents themselves for any change in band shape and position. The porcelain specimens will also be tested for their toxicity and stability to the oral environment.

BIBLIOGRAPHIC REFERENCES: W.T. Wozniak and B.K. Moore, 'Luminescence Spectra of Dental Porcelains,' J. Dent. Res., in press, July (1978).

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

9.0060, DEVELOPMENT OF A SOFT DENTURE LINER FOR PROLONGED USE

D.H. Lewis, Southern Research Inst., Biomaterials Section, *2000 9th Ave. S., Birmingham, Alabama* 35205 (R01 DE 04794-02)

The objective of the research project is to develop a superior soft denture liner for prolonged use. None of the commercial soft-liner materials offers an adequate combination of physical, mechanical, and esthetic properties together with biocompatibility and ease of fabrication. The goal is to develop a material that can easily be fabricated, by intraoral and extraoral methods, into a non-toxic, biocompatible soft denture liner having excellent strength, compliance, wettability, bondability, and resilience, both initially and after prolonged use, and offering resistance to staining, microbial growth, and accumulation of odor and taste. Several chemical classes of polymers including commercial and developmental systems are under investigation for this application. The study includes both in vitro and in vivo evaluations.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $44,767

9.0061, NATURE OF ALLOY SYSTEMS FOR CROWN & BRIDGE RESTORATIONS

K. Asgar, University of Michigan, Ann Arbor Campus, School of Dentistry, Dept. of Dental Materials, *Ann Arbor, Michigan* 48104 (R01 DE 04883-02)

The foremost research objectives of this project involve the conception and formulation of new materials, or modifications of already existing materials, in order to improve the quality of crown and bridge prostheses both in procelain-metal restorations as well as those made of complete cast pieces. In a broad concept this proposal involves: (1) studying the tarnish resistant properties of a Au-Pd-Ag-Cu alloy system in vivo and correlating them to in vitro tests; (2) studying the castability, fit, and solderability of cast restorations of the above system; (3) studying the nature of the metal-porcelain interface, identification of compounds, and strength of the metal-porcelain interface; (4) esthetic quality of procelain restorations of the Au-Pd-Ag-Sn-In system as well as that of the Pd-Ag-Sn-In and base metal alloy system; (5) possible modification of centrifugal casting machines in order to obtain a better and more complete cast piece when lower density alloys, such as alloys of Pd-Ag systems and base metals, are used; and (6) modification or alteration of the composition of dental investments to produce the necessary and required expansion of the mold cavity to compensate for the shrinkage of cast base metal alloys.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $130,351

9.0062, CONSTITUTION DIAGRAMS FOR ALLOYS OF THE NOBLE METALS

R.M. Waterstrat, American Dental Assn., Health Foundation, Research Unit, *211 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 05031-03)

The development of new dental alloys relies heavily on the availability of basic data on the constitution and structure of the various binary alloy systems. Ideally, this data should comprise information on all possible binary combinations. The industry, however, uses rare and expensive materials such as gold or the noble metals which are of little interest to many other industrial users. Thus, the alloys of interest in dentistry are not likely to be of great interest elsewhere and, consequently, there is a serious lack of data such as 'phase diagrams'. This study attempts to supply such data in a systematic manner and in a form which is most convenient to the designer of new alloys.

BIBLIOGRAPHIC REFERENCES: Equilibrium Phase Fields in the Vanadium-Osmium System by C. Susz, R. Flukiger, J. L. Jorda, J. Muller and R. M. Waterstrat. Published in J. Less-Common Metals 63:45, 1979.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $42,508

9.0063, IMPROVED BENDING ANALYSIS FOR ORTHODONTIC WIRES

W.A. Brantley, Marquette University, School of Dentistry, Dept. of Dental Materials, *604 N. 16th St., Milwaukee, Wisconsin* 53233 (R01 DE 05226-01)

A theoretical analysis of the cantilever bending test used in the forthcoming American Dental Association Specification for orthodontic wires not containing precious metals will be undertaken, to develop improved expressions for Young's modulus (E) in bending and flexural yield strength (FYS) which account for the experimentally observed test span length dependence of these bending properties Direct experimental measurements of elastic deflection curves for test specimens with varying length; cross section dimensions ratios will be compared to theoretical predictions from assumed bending deformation models, and photoelasticity techniques may be employed to map stress distributions associated with the actual loading conditions. If improved expressions developed for these bending properties are intractabe for practical use, then curves for E and FYS as functions of length: cross section dimensions will be established for ranges encountered in testing of orthodontic wires. Results from this investigation not only will have direct application towards a future revision of the aforementioned specification, but also be of widespread use for general mechanical testing of engineering materials.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $14,740

9.0064, DENTAL PORCELAIN IMPROVEMENT WITH INORGANIC POLYMERS

C.P. Mabie, American Dental Assn., Health Foundation, Research Unit, *211 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 05353-02)

Improved dental porcelains are being developed from frit grain prepared by the gel route. Emphasis is being placed upon the development of porcelains which exhibit less technique sensitivity during fabrication. An accessory objective is to extend this technology to the preparation of dental abrasives, cements, and fillers.

Gel-route frit preparation procedures involve gelling nitric-acid peptized silica and alumina sols with various solubilized alkali oxides and oxides of Zn, P, Y, Yb, Sm, La, Ti, Ta, Zr, and Sc. Gelled frit is calcined and then ground to prepare the raw porcelain.

Experimental metal-ceramic body porcelains with low solubilities and fusion temperatures, 900-930 degrees C, are being developed. A low solubility glaze which fuses at 871 degrees C, is being developed to strengthen metal-ceramic porcelains.

For the dispersion-strengthening of porcelains quartz, and alumina grains and glass fibers are being dispersed into gels. Attempts are being made to fabricate micaceous porcelains that are stronger and more machineable.

Porcelains with low working range temperatures are being developed so that interfacial stresses can be readily relaxed. Additive laws based upon composition are being sought which predict porcelain properties so that better porcelains can be formulated.

BIBLIOGRAPHIC REFERENCES: Mabie, C. P. and Menis, D. L., Microporous Glassy Fillers for Dental Composites, Journal of Biomedical Materials Research, Vol. 12, 435-472 (1978).

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $29,867

9.0065, SELF-ACTIVATING DEVICES FOR CLEFT-PALATE CHILDREN

R.P. Kusy, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Orthodontics, *Chapel Hill, North Carolina* 27514 (R23 DE 04707-03)

Presurgical orthopaedic techniques are often used as part of the management of cleft-palate children. Previous investigators have attempted to ameliorate such craniofacial anomalies by some form of intra or extra-orally activated appliances. However because of the erratic cooperation of parents to manually activate such appliances the ever-rising expense of in-hospital care, and the need to streamline the physician's role, an alternative solution would be desirable. The objective of this research is to design, from both conventional and novel materials, a self-activating device for treating unilateral and bilateral cleft-palate children. As a first step, a device is proposed which can be programmed to automatically expand the maxillary segments so that the premaxilla may be retracted to properly align with the rest of the alveolar ridge. Preliminary laboratory investigation will involve a stainless steel appliance in which a coaxial spring arrangement is activated by the 'programmed' failure of an irradiated water soluble polymer. By using strain gages and other testing machines, for the first time the magnitude of the forces required to move the bony tissue of the palate will be measured. Appliance fabrication will be developed on the philosophy that each case is unique and requires specific internal hardware which would control the force and displacement requirements. At the same time, however, the external hardware would be universal in design to better accommodate the patient's needs. Clinical assessment will be made first on dogs and later with humans at three different sites. The success of such a project relies on the cooperation of an interdisciplinary team in which engineering plays a key role.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,

National Inst. of Dental Research	$10,502

9.0066, BIOLOGICAL SPECIFICATION OF DENTURE BASE MATERIALS AND DESIGNS

K.K. Kapur, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *16111 Plummer St., Sepulveda, California* 91343 (665-001-P)

Sufficient progress has been made in three areas of this research program.

Over 925 lateral and 426 frontal craniofacial cephalometric radiographs have been traced and checked for accuracy. Of these 537 have been digitized and electronically plotted to clarify and correct digitizing errors.

The effects of age and dentition status on cortical thickness of the inferior mandibular border was studied in two age-matched groups of subjects with complete natural dentition and complete dentures. Cortical thickness and cortical areas of the inferior border were found to be significantly smaller in denture wearers than in the group with natural dentition. No significant trend with age was noted in either dentition group. This study will be extended to include Kennedy Class and Class II partially edentulous patients.

Emg activity and masticatory performance tests have been completed on six denture wearers under four different denture base fit conditions. The testing on the remaining 19 patients should be cmpleted by the end of December, 1979.

The instrumentation for measuring pressures placed on denture bearing support during chewing has been completed. Transducers have been placed in a set of duplicate dentures, which have been subjected to similar adjustments as the original dentures. The pressure measurements in this subject will be made within the next month. After the methodology is trial tested and standardized, additional subjects will be studied.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

9.0067, FUNCTIONAL LOADING OF BIOCERAMIC AUGMENTED ALVEOLAR RIDGE

E.B. Nery, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Research Section, *5000 W. National Ave., Wood, Wisconsin* 53193 (695-008-F)

Two adult mongrel dogs were used in this study. Mandibular right posterior teeth were extracted. The wound was allowed to heal for two months, followed by augmentation with porous tribasic calcium phosphate ceramic. In order to determine the effects of a denture over the augmented site, a unilateral, distal extension, removable, partial denture was constructed and inserted. At the end of a six-month period, clinical evaluation revealed a healthy alveolar ridge tissue with no inflammatory reaction due to implant. Histological examination confirmed the clinical findings; that is, no inflammation, bone and soft tissue grew into the pores, and no bone resorption occurred. It is concluded, therefore, that porous tribasic calcium phosphate ceramic is a potential material for alveolar ridge augmentation.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

9.0068, A CLINICAL AND LABORATORY EVALUATION OF BASE-METAL ALLOYS FOR DENTAL RESTORATIONS

H.F. Morris, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Southfield & Outer Dr., Allen Park, Michigan* 48101 (553-001-P)

Variations in the reported mechanical properties for various based-metal removable partial denture alloys are common. Using test samples cast from the same batch of alloy under specific conditions by three large government laboratories resulted in significant differences in the mechanical properties obtained. All test samples were visually acceptable. One laboratory produced casting that were so inferior that testing was not possible. The other two laboratories provided test samples with properties ranging from 81,000 psi to 88,000 psi (0.02% y.s.) and 100,000 to 102,000 psi for the 0.2% y.s. Ultimate tensile strengths of 124,000 psi were recorded for the two groups with an elongation of from 5% to 8%. Simple means of monitoring the casting in large dental laboratories has evolved from this study that will help in the quality control of thousands of castings made each year.

PAPERS PRESENTED: I.A.D.R. Meeting, New Orleans, March 28-30, 1979: 1) Polished vs non-polished clasp behavior; 2) A simple method of monitoring the castings in large laboratories; 3) Progress report: Three (3) year evaluation of Base-Metal Crown and Bridge Alloys.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

9.0069, STRESS ANALYSES OF ANTERIOR FIXED PROSTHESES

D.G. Jochen, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Central Dental Laboratory, *Wilshire & Sawtelle Blvds.*, *Room 209, Los Angeles, California* 90073 (691-002-F)

Assertions of the desirable features of metal framework designs for porcelain fused-to-metal (PFM) restorations have been largely based on empirical evidence. Little hard data has been presented concerning the load transfer characteristic of the conventional bar and trestle anterior fixed bridge framework designs. The purpose of this investigation was to photoelastically compare the stresses induced in bar and trestle anterior PFM frameworks.

This study utilized a three unit fixed bridge extended from canine to central incisor. Abutment teeth, and subsequent frameworks, were reported approximately four times natural size in photoelastic plastics. Connector dimensions and location were the same for both framework designs. The model frameworks were cemented to the abutment teeth and were subjected to occlusal loads at the pontic. The resultant stresses were locked into the models using stress freezing techniques. The stress frozen models were observed and photographed in a circular polariscope before and after sectioning.

The specific occlusal load applied to the pontics produced bending and torsional stresses at the connectors in both frameworks, with the central pontic tending to be more highly stressed. The trestle design was generally less highly stressed and exhibited a more uniform distribution of stress within the connectors.

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Medicine & Surgery funds n.a.

9.0070, ESTHETIC COLOR MATCHING AND BLENDING IN CERAMIC DENTAL RESTORATIONS

K.R. Thompson, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *S. 1st St., Temple, Texas* 76501 (674-001-P)

Remaking ceramic restorations due to inaccurate color matching has resulted in considerable time loss for dentist, technician and patient. A standardized system of communication in color matching and blending between the dentist and technician is needed.

Initially, color slides were projected on an Ada viewer utilizing gelatin filtration in the path of light. The goal was standardization with Kodak color standards.

The Ada projector has been ineffective, and in future cases, a standard Kodak slide projector will be utilized with gelatin filtration placed in front of the objective lens.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

DIAGNOSIS & TREATMENT - IMPLANTS

9.0071, DEVELOPMENT OF BIODEGRADABLE IMPLANTS FOR USE IN MAXILLOFACIAL SURGERY

D.R. Cowsar, Southern Research Inst., *2000 9th Ave. S., Birmingham, Alabama* 35205 (DAMD17 78 C 8059)

Investigators propose to develop high-strength resorbable materials for use in the management of avulsive maxillofacial injuries.

The investigators plan to investigage multiple chemical and physical approaches for producing resorbable implant materials with superior values of mechanical strength. New and old polymers will be synthesized of high molecular weight and exceptional quality. Also investigated will be physical approaches to the development of high-strength materials such as drawing and annealing the polymers at elevated temperatures, reinforcing them with fibers and laminating multicomponent materials.

SUPPORTED BY
U.S. Dept. of Defense, Army,
Medical Research &
Development Command $49,627

9.0072, SURGICAL TOOTH IMPLANTS, COMBAT AND FIELD

C.R. Hassler, Battelle Memorial Inst., *505 King Ave., Columbus, Ohio* 43201 (DADA17-69-C-9181)

Develop a porous surfaced ceramic root structure that will allow an anchoring tissue ingrowth and with a metallic core that will support a dental crown. Design new root form implants that will facilitate the technique of implanting and allow higher load bearing capabilities than the present state-of-the-art allows. Conduct an implant program to evaluate the preceding concepts. This study is of extreme military importance as successful completion will result in reduction of dentists time spent in full and partial denture construction and provide on the spot replacement for over a quarter of a million of teeth lost by Army personnel per year. There will be drastic reduction in cost of treatment time, laboratory fabrication, and cost of materials.

Ceramics and ceramic-coated materials will be formulated which will be intended to function as permanent replacements for lost teeth. The new materials will be cast in root form with a controlled surface porosity which will allow fibrous attachment to the surrounding bone. An in-vivo evaluation study utilizing rhesus monkeys will follow as new techniques and materials are developed.

SUPPORTED BY

U.S. Dept. of Defense, Army,
Medical Research &
Development Command,
Dental Research Div. $4,490

9.0073, USE OF METALLIC ENDOSSEOUS IMPLANTS AS A TOOTH SUBSTITUTE

M.B. Weiss, Rush Presbyterian St. Lukes Medical Center, *1753 W. Congress Pkwy., Professional Bldg. 907, Chicago, Illinois* 60612 (DAMD17 77 C 7021)

The objective is the development of a biologically and technically feasible total replacement for missing teeth. Over a quarter million teeth per year are lost by military personnel. Success in this study will provide an alternate means to replace lost teeth and negate the requirement for bridges and other prosthetic devices. There will be a reduction in clinical treatment time, reduction in laboratory fabrication time and considerable monetary savings.

Sintered metallic fiber tooth root structure implants of vitallium will be produced. These structures will be implanted into the socket of the missing tooth. The arrangement of the sintered fibers will allow permanent attachment of ingrowth of bone. An in vivo evaluation study in laboratory animals will follow as techniques and materials are developed.

SUPPORTED BY

U.S. Dept. of Defense, Army,
Medical Research &
Development Command,
Dental Research Div. funds n.a.

9.0074, EVALUATION OF DENTAL IMPLANTS AS APPLIED TO NAVY AND MARINE CORPS PERSONNEL

J.E. Yeager, U.S. Dept. of Defense, Navy, Naval Dental Research Inst., Clinical Investigation Dept., *Great Lakes, Illinois* 60088 (DN677137)

TECHNICAL OBJECTIVE: Degenerative and destructive dental diseases, oral tumors, avulsive missile wounds sustained in combat, and accidental injuries which cause tissue loss result in significant reconstructive treatment problems among those Navy and Marine Corps personnel who cannot be treated by conventional prosthetic measures. The purposes of this study are to improve the best currently used methods and to develop innovative techniques for the surgical and prosthetic reconstruction of bone deficient jaws.

APPROACH: Dental and bone implants will be evaluated in monkeys to determine which procedures, materials and designs are most feasible for testing and possible later routine use in human subjects.

PROGRESS: A comparative evaluation in monkeys of four implant materials - a surgical grade chrome/cobalt alloy, vitreous carbon, acrylic and aluminum oxide - is being completed. A clinical finding was that the surgical grade chrome/cobalt alloy and vitreous carbon were superior to acrylic and aluminum oxide as materials used for functional, artificial tooth root replacement devices. Laboratory animals are now being prepared for dental implant design testing.

SUPPORTED BY

U.S. Dept. of Defense, Navy,
Naval Medical Research &
Development Command,
National Naval Medical Center funds n.a.

9.0075, IMPLANT FIXATION IN BONE BY ELECTRICAL STIMULATION

J.B. Park, Clemson University, School of Engineering, Dept. of Interdisciplinary Studies, *Rhodes Research Bldg., Clemson, South Carolina* 29631 (R01 AM 19828-03)

The purpose of the proposed study is to determine the extent to which electrical potentials can influence osteogenic activity in porous coated implant materials. The growth of tissue into porous implants has been well established as a feasible means of attaching load-bearing prosthesis to the musculo-skeletal system. Attachment by in growth eliminates most of the problems associated with other means of fixation, but has itself the disadvantage that the patient must be immobilized for long periods of time to permit sufficient ingrowth to ensure stability.

The stimulation of bone by imposed electrical potentials has been demonstrated for fracture healing and for some 'preliminary' bone growth into porous coated implants. The proposed study is directed to broaden our knowledge of the effect of electrical stimulation on: (1) the actual interfacial strength of implant/tissue union; (2) the kinetics of tissue ingrowth and (3) the morphology of the union.

Carefully sectioned push-out specimens will be made to test the strength of the unions and comparisons will be made between the electrically stimulated and non-stimulated control samples along the length of the femur. The kinetics of tissue ingrowth will be determined quantitatively by a conmbination of wet chemical assaying and microscopic techniques.

A porous polymer (polymethylmethacrylate) and metal (CouCr-Mo alloy) that are sintered to a solid metal core approximately 2 mm thick will be implanted in the intramedullary cavity of canine femurs since these materials are being investigated for their usefulness as porous implant materials in orthodpedic and dental application by the principal investigator.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Arthritis Metabolism & Digestive Diseases	$47,252

9.0076, INCREASED WEAR RESISTANCE OF ULTRA-HIGH MOLECULAR WEIGHT POLY(ETHYLENE) (UHMWPE)

R.P. Kusy, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Orthodontics, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130112)

The objective of this project is to enhance the wear properties of UHMWPE for use in such biomedical applications as the acetabulum component in the total hip prosthesis. Stabilization of a commercially manufactured UHMWPE will be achieved by the modification of the molecular weight distribution. Abrasion tests will be utilized to evaluate the modified versus unmodified material.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$12,574

9.0077, TISSUE-MATERIAL INTERACTION IN IMPLANT MATERIALS

D.F. Taylor, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Operative Dentistry, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130179)

The objective of this project is to develop improved implant materials by improved understanding of their interactions with tissue. The materials under investigation include ceramic matrix and polymer matrix composites. They generally include both pores for tissue ingrowth and high modulus fibers for reinforcement. Two areas of research are active at this time. The first is the in-vivo evaluation in mandibular sites in dogs of a series of materials. The materials are all placed as totally buried tooth-root implants in fresh molar and premolar extraction sites. The materials under investigation have been chosen on the basis of prior favorable behavior in femoral sites. The second active research area is related specifically to polymer matrix composites. Reinforced with high modulus poly-imide fibers, these materials are capable of matching the modulus of elasticity of bone. Present activity is directed toward computer modelling of the polymerization reactions in methacrylate polymers. An extreme number of composition variations are possible in these materials. The modelling procedure is expected to greatly reduce the number of formulations requiring clinical evaluation.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$27,922

9.0078, ARTIFICIAL TOOTH ROOTS

F.A. Young, Medical University of South Carolina, School of Dentistry, Dept. of Biophysical Dentistry, *Charleston, South Carolina* 29401 (R01 DE 03497-07)

Artificial tooth roots of sintered porous titanium are being evaluated in Rhesus monkeys as supports for crowns and bridges. The times of function range from 1 to 5 years. Crowns and bridges are evaluated clinically and histologically. Single crowns are unsupported and free standing without mesial or distal contacts. Bridges are supported by an implant and one natural tooth or by two implants. The restorations are fully in occlusion and function.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$89,914

9.0079, CARBON DENTAL IMPLANTS

L.B. Shulman, Harvard University, Boston Campus, School of Dentistry, Dept. of Oral Surgery, *188 Longwood Ave., Boston, Massachusetts* 02115 (R01 DE 03755-06)

Evaluation of Vitreous Carbon Tooth-Root Implants (Vitredent design) in baboons will continue until all implants have been at risk for five years (1979). In conjunction with researchers from the Bioengineering Department of the Rensselaer Polytechnic Institute, measured stresses will be applied to a selected number of these implants and the pattern of implant deflection traced. Evaluation of the safety and efficacy of the Vitredent implants in humans will continue; ultimately 50 implants will be placed and restored in these clinical trials, involving mandibular single interdental and distal abutment applications of this implant. Histologic evaluation of nonfunctional rods of five materials placed subgingivally in edentulous areas of Vervit monkeys will be carried out; comparisons will be made between tight and loose fitting rods.

BIBLIOGRAPHIC REFERENCES: Schnitman, P.A. and Shulman, L.B.: Dental Implants - Their Current Status. J. Mass Dent Soc. 26(4):278-286, Fall, 1977.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

9.0080, POROUS METAL DENTAL ANCHORS IN LONG-TERM FUNCTION

R.E. Westerman, Battelle Memorial Inst., Pacific Northwest Laboratories, *P.O. Box 999, Richland, Washington* 99352 (R01 DE 03938-05)

The objective of this program is the evaluation of the long term behavior of endosteal porous metal dental implants used in full function as tooth replacements in macaque nemestrina monkeys. Prosthesis stability is achieved by bone ingrowth into the Void-Metal-Composite (VMC) implant, a porous titanium alloy base material. Gold crown restorations attached to the VMC implants allow the prosthesis to be evaluated under the stresses of full occlusal function.

The VMC implants are of cylindrical shape, and made of Ti-6A1-4V alloy with interconnecting pores of 450micron diameter.

We are currently proposing a continuation of our existing grant into the fifth program year. A total of 18 animals, carrying 78 implants, 68 of which are crowned, are involved in the studies. Implant times range from 1/2 to 3 years, as of 2-79.

The performance of the implants to date is highly encouraging, with an observed failure rate of less than 10 percent. The planned activities for the fifth program year include sacrifice of three animals, one of which will have an accrued implant time of 4 years.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $49,424

9.0081, A STUDY OF SUBPERIOSTEAL ORAL IMPLANTS

J.R. Natiella, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Pathology, *3435 Main St., Buffalo, New York* 14214 (R01 DE 04226-04)

An experiment is proposed that would test two types of unilateral subperiosteal oral implants under external loads applied through fixed prosthodontics in a primate model. Cast Surgical Vitallium frameworks will be coated with a microporous tissue interface material of polyurethane. The tissue repair and regeneration to this surface will be compared with non-coated implants that have received a glow-discharged surface treatment. A similar comparison will be made between implants placed in long bone and subcutaneous sites. Tests to demonstrate optimum bonding of porous materials to metal implants are component of this study. Surface chemical and physical methods will be used to assess tissue acceptance and characterization of pre- and post-implant surfaces.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $119,685

9.0082, POROUS HIGH-DENSITY POLYETHYLENE TOOTH ROOTS

M. Spector, Medical University of South Carolina, School of Dentistry, Dept. of Biophysical Dentistry, *Charleston, South Carolina* 29401 (R01 DE 04414-04)

Porous high density polyethylene (PHDPE) coated tooth roots which have successfully served as abutments for individual free standing posterior teeth in dogs will be employed as abutments for free standing anterior and posterior teeth, and as distal abutments for 3 unit posterior bridges in monkeys. One objective is to determine if the biological response of the primate alveolar bone to the PHDPE coated tooth roots is similar to that of the dog. Previous studies using porous titanium implants of a similar design suggest that more bone forms in the primate implants than is formed in canine roots. It will be important to establish if there is a species difference in the biological response to porous artificial tooth roots. A second objective is to determine whether implants which have functioned successful as free standing single posterior tooth replacements in masticatory function can serve as well under occlusal function (as abutment for bridgework) and can serve in areas which receive higher lateral loads (anterior teeth).

A third objective of the present research is to delineate the modes of failure of the porous coated tooth roots. The study will primarily address two potential modes of failure; catastrophic mechanical failure due to masticatory loads which cause failure at the PHDPE/bone interface and periodontal disease processes. The former mode of failure will be investigated experimentally by loading to failure eight in plants each at 3 and 12 months. Periodontal disease processes will be identified using transmission electron microscopy in conjunction with histological evaluation of specimens obtained by biopsy and autopsy. A final objective is to determine if the mechanical properties of the porous coating (e.g., modulus of elasticity) influence the biological response and hence clinical performance of the implants. This objective will be achieved by comparing results of the PHDPE studies with results of studies of porous titanium implants having the same design (these latter studies are presently being conducted in the principal investigator's laboratory under another NIDR research grant).

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $88,190

9.0083, A COMPARISON OF A1Z03 AND CARBON DENTAL IMPLANTS

J.J. Klawitter, Tulane University of Louisiana, School of Engineering, Dept. of Mechanical Engineering, *New Orleans, Louisiana* 70118 (R01 DE 04653-03)

The objectives of this research are two fold: 1) to determine the effect that variations in material elastic modulus has on the performance of dental implants, and 2) comparatively evaluate Al_2O_3 and pyrolytic carbon as materials of construction for dental implants. Blade type implants of the same size and shape fabricated from pyrolytic carbon, Al_2O_3 and carbon coated Al_2O_3 will be implanted in baboons for 1/2 years. Post sacrifice mechanical, histological and microradiographic analyses will be performed. Finite element stress analyses will be conducted to determine stress distributions and implant displacements during loading. The results of the analytical treatment and animal testing will be compared.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $51,871

9.0084, BIOLOGICAL PROSTHETIC ATTACHMENT

J.J. Klawitter, Tulane University of Louisiana, School of Engineering, Dept. of Mechanical Engineering, *New Orleans, Louisiana* 70118 (R01 DE 05292-01)

The research program centers on determining the interface mechanics between biomaterials and bone. The objective of the research is to use experimentally determined information together with the results of finite elements stress analyses to optimize the bone-biomaterial interface design of experimental femoral head prostheses. The materials to be studied are porous materials intended for bone ingrowth and surface active bioglass materials intended to achieve chemical bonding to bone. Experimental determinations of the interfacial deformation characteristics will be made, using experimental animals, as the function of pore size and depth of porous coatings. Similar measurements will be made for the bioglass material. Finite element stress analyses will be performed using an analytical model corresponding to the geometry of the mechanical test specimens, providing a feedback loop which will be used to evaluate and refine the assumptions and validity of the model. The results from the mechanical testing and stress anaylsis phases will be used to optimize the interface design of femoral head prostheses having a porous coating and bioglass coating. Femoral head prostheses will then be fabricated, implanted and evaluated in animals.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $84,038

9.0085, CONFERENCE ON DENTAL IMPLANTS - BENEFIT OR RISK

P.A. Schnitman, Harvard University, Boston Campus, School of Dentistry, Dept. of Prosthetic Dentistry, *188 Longwood Ave., Boston, Massachusetts* 02115 (R13 DE 04860-01S1)

The clinical efficacy of dental implants remains unclear because of a dearth of sound clinical data. Scientific animal and clinical research is new to this field; extremes of opinion have been dominant to date. This conference is designed to congregate the expert and the experienced in implant dentistry in an academic setting to concentrate on matters of clinical benefit and risk; the aim is to assimilate as much clinical knowledge as is currently available into a rational concensus. The conference will be divided into three sessions, one devoted to each major type of implant in current clinical use: subperiosteal-transosteal, Vitredent and blade. In each session two recognized proponents of benefit and risk respectively will present their views in a forty minute debating-type format. The audience, composed of thiry-five invited experts, will then discuss the presentations for a full hour, using their own data in evidence. A workshop to develop concensus positions on implant prognosis will follow. The entire proceeding will be recorded and published for dissemination to the dental profession at large.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $10,433

9.0086, DENTAL IMPLANT FIXATION BY ELECTRICALLY MEDIATED PROCESS

J.B. Park, Clemson University, School of Engineering, Dept. of Bioengineering/Materials Engineering, *Rhodes Research Bldg., Clemson, South Carolina* 29631 (R23 DE 04712-03)

The proposed research is to determine the effect of electrical stimulation on the tissue growth into porous dental root with a solid core. In addition, the healing characteristics of the gingival cervix affected by the electrical stimulation will be studied.

To simplify the experiment two types of implants (subgingival and transgingival) will be made from polymethylmethacrylate. The subgingival (1.05 cm long X 0.45 cm dia.) and transgingival implants will be identical except that the latter will have a solid neck portion (0.38 cm long X 0.25 cm dia) protruding through the mucosa. The electrode (Pt-13%Rh) will be wound around the solid root core (0.8 cm long X 0.25 cm dia.) before porous portion is made.

The implants with negative electrode will be placed in the distal root socket of the 4th premolar of dogs. The other electrode will be buried in the alveolar bone distal to the third premolar. The stimulation will be done at one current level (approximately 4 micron A) by using an 1.4V mercury battery with a resistor in series encapsulated by silicone elastomer.

In addition to the conventional clinical evaluation of the implant the actual strength of the implant/tissue interface will be determined by using a pull-out test on an Istron machine. The quantification of the amount of tissue grown in the pores by chemical assaying and microscopic examination will be correlated to the strength of the interface for both stimulated and non-stimulated control specimens.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $21,157

9.0087, IN VIVO FORCES ON ENDOSSEOUS DENTAL IMPLANTS

J.B. Brunski, Rensselaer Polytechnic Inst., School of Engineering, Dept. of Biomedical Engineering, *110 8th St., Troy, New York* 12181 (R23 DE 05418-01)

Biomechanical variables including the masticatory forces on a dental implant, the implant geometry, and the resulting stresses and strains in interface tissues can determine the clinical success or failure of an endosseous dental implant. Up to now, inadequate characterization of masticatory forces on dental implant in various animal models has held back development of biomechanical design principles for dental implants. It is the goal of this research to measure in vivo forces on dental implants as functions of (1) bridgework over the implant and (2) the animal model.

In the first year of the grant the aim will be to measure only the apical force component on a dental implant in vivo. To perfect the technique, a convenient implant geometry will be instrumented with strain gages, calcibrated, and then implanted into beagle dogs. Wires from the gages will be routed subcutaneously to each animal's back, and connected to appropriate bench-top electronics. Procedures will resemble those used by other workers who successfully measured in vivo strain in canine bones by strain gage methods.

In years 2 and 3 of the grant, the aim will be to apply the methods developed in Year 1 to investigate how the force components in general on a dental implant depend upon (1) the type of bridgework over the implant, and (2) the animal model. To attack the latter problem completely, a commercially-available implantable telemetry system will be adapted for use with instrumented implants, since hard-wiring will be impractical in animals such as baboons or monkeys that are commonly used in implant research.

Development of the capability to measure in vivo forces on dental implants in various animal models will lead to future experiments aimed at defining the interactions between implant-tissue biomechanics and clinical performance of implants.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $18,718

9.0088, INTERFACIAL BEHAVIOR OF BIOMATERIALS

L.L. Hench, State University System of Florida, University of Florida, School of Engineering, Dept. of Materials Science & Engin, *220 Black Hall, Gainesville, Florida* 32611 (R01 GM 24858-02)

The objectives of this project are: 1) Describe and understand the interactions of bone cells, skin firbroblasts, lymphocytes, and macrophages with the surfaces of bioglasses of varying composition and surface characteristics; and 2) Establish a scientific basis for in vitro evaluation of toxicity and bondability of controlled surface active materials considered for use as implants.

Sensitive quantitative assays for alkaline phosphatase and cAMP have been established. The specific activity of alkaline phosphatase in bone cell culture were approximately 10X that in skin fibroblasts. Bone cells in vitro were shown to produce elevated levels of cAMP in response to treatment with either PTH or calcitonin.

Growth rates, cell saturation densities, and alkaline phosphatase activities for both bone cells and skin fibroblasts cultured on control substrates compared with bioglasses show no evidence of toxicity. However, the bioglasses develop strong adherence between the cell layer and the active calcium phosphate film forming on the material similar to in vitro bone bonding behavior of these materials.

Mechanisms of cell adherence to the bioglasses, evidence for intercellular mineralization in vitro, additional assays for collagen synthesis and macrophage phagocytosis will be studied as a function of composition of the surface active layers on bioglasses. Confirmation that there is no evidence of bioglass toxicity for normal human lymphocytes comparing RNA synthesis of bioglasses and controls will also continue.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of General
Medical Sciences $100,838

9.0089, COOP STUDY NO. 86 - DENTAL IMPLANTS

K.K. Kaur, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *16111 Plummer St., Sepulveda, California* 91343 (665-003-P)

The investigators from all the five participating VA Medical Centers received formal clinical training in the placement of implants and their research dental assistants in data collection procedures. Each investigator independently inserted 6 to 8 implants in non-study patients. Three of the five centers (San Diego, Sepulveda and LAOPC) have started entering patients into the study. The two other centers are completing the pre-entry requirements including collection and submission of duplicate measurements on 10 non-study patients.

As of this date, 18 patients have been randomized for the study. An additional 16 patients will be entered shortly. the Sepulveda VA Medical Center has entered 8 patients into the study. Eight additional patients have been screened and will be submitted for entry within the next few weeks.

Although the number of patients entered in the study is lower than originally anticipated for 6 months, we expect to meet the required number by 24 months.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

9.0090, SINTERED TITANIUM FIBER IMPLANTS FOR MANDIBULAR RIDGE AUGMENTATION

D.M. Laskin, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *820 S. Damen Ave., Chicago, Illinois* 60612 (537-001-P)

A previous study has shown osseous growth into sintered titanium fiber mesh when implanted subperiosteally. In this study, the practicality of its use for mandibular ridge augmentation was explored. Using a die, titanium fiber was pressed into rectangular box shapes approximately 42% dense, and then sintered. Twelve adult mongrel dogs were made edentulous with radical alveolectomy in the posterior maxilla and mandible bilaterally. After 8 weeks the implants were placed subperiosteally on the edentulous mandibular ridges via an intra-oral approach and secured with titanium screws. The dogs were given 10 mg/kg of tetracycline I.V. one week prior to sacrifice. Two dogs were sacrificed at 1, 3, 6, 9, 12, and 24 weeks. The methyl methacrylate embedded specimens were studied by radiography and conventional and fluorescent microscopy. Osseous ingrowth from the alveolar ridge was maximum at 3 weeks and penetrated the implant to a depth of 300 microns in some areas. This bone remodeled over the subsequent periods but remained at the 200 micron level. The surfaces of the implant contacting the underside of the periosteum became encapsulated. Clinically, the implants were well tolerated without infection, dehiscence or rejection. Based on these findings, investigation of sintered fiber mesh as an augmentation material in man is warranted.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery funds n.a.

9.0091, EVALUATION OF DURAPATITE AS AN IMPLANT MATERIAL IN PATIENTS WITH PERIODONTAL LESIONS

I.W. Scopp, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *1st Ave. at E. 24th St., New York, New York* 10010 (630-002-P)

Periodontal lesions are extremely common, affecting well over half of the general population. The currently acceptable treatment, consisting of planing, scaling, debridement and currettage, is prolonged and expensive. Recently, some success has been achieved in filling advanced, destructive periodontal defects with autogenous marrow and cancellous bone from the iliac crest, or by an osseous coagulum from the mouth. It is the purpose of this study to compare treatment with durapatite with controls in patients with bilateral lesions of the same size. The controls will be treated by conventional therapy. Durapatite is a dense polycrystalline form of hydroxylapatite and is free of fine pores and secondary crystalline phases. The material has a significantly greater compressive strength than previously reported sintered hydroxylapatites. A 'split-mouth' study design will be employed on 30 patients. By random assignment all advanced periodontal defects on one side of the mouth (lower and upper) will be treated by durapatite implant (preceded by debridement), while similar defects on the contralateral side will be treated by conventional therapy only. The patients will be observed for two years.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery funds n.a.

9.0092, HUMAN PERIODONTAL TISSUE REACTION TO A POROUS CERAMIC BONE SUBSTITUTE

W.B. Gillette, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *1481 W. 10th St., Indianapolis, Indiana* 46202 (583-001-P)

The purpose of this study is to evaluate the human gingival tissue response to a resorbable tricalcium ceramic (Synthos).

Discs 3-4mm in diameter have been implanted between the labial gingiva and bone overlying teeth scheduled for later extraction. Controls are contralateral teeth with autogenous bone fragments implanted. Five patients have been completed to date. Periods between implantation and harvesting the study tissue range from two weeks to three months. Synthos appears to elicit little tissue reaction clinically and histologically. Fibrous connective tissue invades its channels. Osteogenesis is not prominent. Further subjects are being sought. A companion study testing Synthos in patients with active periodontal disease is in progress.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery funds n.a.

9.0093, ELIMINATION OF HUMAN OSSEOUS PERIODONTAL DEFECTS BY A CERAMIC BONE SUBSTITUTE

W.B. Gillette, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *1481 W. 10th St., Indianapolis, Indiana* 46202 (583-002-P)

The resorbable tricalcium phosphate ceramic, Synthos, is used to attempt eradication of one-wall osseous periodontal defects caused by naturally occurring periodontal disease. Only cases not highly amenable to simpler modes of treatment are selected. Control defects will be used where possible and will consist of similar defects in the same patient. One patient has been treated to date with encouraging results. Slow progress is envisioned.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery funds n.a.

9.0094, AN EXPERIMENTAL SYSTEM FOR THE EVALUATION OF THE BIOCOMPATIBILITY OF MATERIALS USED IN DENTAL IMPLANTOLOGY

D.A. Garcia, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *1400 Vet. of Foreign Wars Pkwy, West Roxbury, Massachusetts* 02132 (690-005-P)

The objectives of this study were a) to develop an animal model to test the compatibility of inert materials in bone, and b) to evaluate dental implant materials in this system.

In this model, a material is evaluated separately for its effects on bone formation and resorption.

Two types of bone preparations are inserted into the leg muscles of rabbits: a) cylinders of allogeneic bone matrix, an osteoblastic bone-forming system, and b) devitalized autogenous iliac crest fragments, an osteoclastic resorbing system. Test materials are prepared as cylindrical plugs to fit within the lumens of matrix cylinders and in channels cut into iliac fragments. The specimens are removed after several weeks in situ and ashed to measure bone formation and resorption.

Normal values for each process were establishd for periods of from 2 to 10 weeks in situ. The implant materials Vitallium and poly (methylmethacrylate) (PMMA) were found to inhibit bone formation by 25% and 45%, respectively, but had no effect on resorption. When PMMA was tested at three different levels of monomer content, the degree of inhibition was found to vary with the amount of monomer contained (45%, 52% and 61% inhibition for levels of 25%, 33% and 50%, respectively). PMMA was also prepared containing 100 to 500 micron sized matrix particles and tested. Inhibition was partially reversed by the presence of matrix (26% inhibition vs 45%). It was concluded that the acceptance of implant materials in bone may be enhanced by the incorporation of bone matrix substances in them.

Preliminary results of this study were reported at the annual meeting of the International Association for Dental Research, April, 1979.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

9.0095, TISSUE RESPONSE TO ENDOSTEAL IMPLANTS

C.W. Freidline, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *11201 Benton St., Loma Linda, California* 92357 (605-001-P)

The objectives of this study will be to (1) study in terms of clinical, roentgenographic, histological and histochemical, evaluations, certain individual components of blade implants and the influence of bacterial plaque on variations within these components; specifically, the surface texture and post circumference will be the variables studied; (2) study longitudinally the adhesive mechanisms shown to exist at the interface between cells of the junctional epithelium and the implant surface; and (3) study the development and maturation of the microvasculature of the peri-implant tissues and accompanying cellular changes. It is proposed to implant surgically and stabilize by splinting one multiposted Vitallium blade in each anterior jaw of twelve monkeys. These will be observed and changes measured over varying periods of time. Using block sections, histological and histochemical examinations will be made of the peri-implant tissues. A longitudinal study will determine the length of time required for hemidesmosome formation following implant placement. One-half of the animals used in a longitudinal study will be perfused at time of euthanization. These animals will be used to study the development of the microvasculature while the remaining half will be used to study concomitant cellular changes.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

9.0096, MANDIBULAR RAMAL-SYMPHASEAL IMPLANT DENTAL PROSTHESIS

J.R. Moore, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *800 Stadium Rd., Columbia, Missouri* 65201 (543-001-F)

Our implant project has resulted in a workable implant design which combines endosteal and subprosteal anchoring components to provide the stabilizing elements necessary for lower denture retention. We have used this design in 3 patients at this time, 2 of which have been clinically acceptable for over 2 years. There is, however, a suggestion of the implants loosening in one patient, a situation which must be resolved or implant failure will be imminent. We are learning a great deal in this time regarding factors critical to implant success which we had not envisioned previously. Therefore, we feel that the project is worthwhile and will offer reportable data before long.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

9.0097, THE COMPOSITE ALLOPLASTIC IMPLANT

R.E. Holmes, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Plastic Surgery Service, *4500 S. Lancaster Rd., Dallas, Texas* 75216 (549-002-P)

In a preliminary study the unique biogenic microarchitecture of the Scleractinian coral P. porites, converted to pure hydroxyapatite (CHAP), was used as a bone graft substitute in the dog mandible. Complete bone regeneration was documented at 6 months. Based on this promising finding a study protocol to compare the quantity of bone regeneratin in CHAP implants vs. autogenous bone grafts in four animal models has been initiated. The models are: 1) alveolar augmentation and intraoral onlay, 2) craniofacial augmentation and cranioplasty, 3) radial inlay and 4) spinal fusion. A total of 80 dogs (20 in each group) have been entered into the study and 2 month specimens have recently been harvested. Later specimens will be harvested at 4, 6, 12 and 24 months. All dogs receive tetracycline daily after surgery to label regenerated bone. Fluorescent image analysis of petrographic sections will be used to quantitate bone regeneration. A model for biomechanical strength measurements of regenerated bone in CHAP implants is currently under development.

In a preliminary study of a microvascular prosthesis the biogenic microarchitecture of the echinoderm H. trigonarius (EST) was used to fabricate a silastic vessel 1.0 mm I.D. In 35 rats the abdominal aorta was replaced and specimens were harvested at intervals up to 6 months. An overall patency rate of 88% was found. Based on this promising finding a study protocol to compare neointimal regeneration in EST vs. autogenous vein grafts has recently been initiated. Histology, SEM, electromagnetic flow and angiographic techniques will be used for evaluation.

BIBLIOGRAPHIC REFERENCES: Holmes, R.E.: Bone regeneration within a coralline hydroxyapatite implant. Plast. Reconstr. Surg. 63:626, 1979.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

9.0098, THE COMPOSITE ALLOPLASTIC IMPLANT

R.E. Holmes, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Plastic Surgery Service, *4500 S. Lancaster Rd., Dallas, Texas* 75216 (549-001-P)

In a preliminary study the unique biogenic microarchitecture of the Scleractinian coral P. porites, converted to pure hydroxyapatite (CHAP), was used as a bone graft substitute in the dog mandible. Complete bone regeneration was documented at 6 months. Based on this promising finding a study protocol to compare the quantity of bone regeneration in CHAP implants vs. autogenous bone grafts in four animal models has been initiated. The models are: 1) alveolar augmentation and intraoral onlay, 2) craniofacial augmentation and cranioplasty, 3) radial inlay and 4) spinal fusion. A total of 80 dogs (20 in each group) have been entered into the study and 2 month specimens have recently been harvested. Later specimens will be harvested at 4, 6, 12 and 24 months. All dogs receive tetracycline daily after surgery of label regenerated bone. Fluorescent image analysis of petrographic sections will be used to quantitate bone regeneration. A model for biomechanical strength measurements of regenerated bone in CHAP implants is currently under development.

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SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

9.0099, PREPARATION AND IMPLANTATION STUDIES OF PHOSPHATE CERAMIC

A.A. Grant, University of Manchester, Turner Dental School, *Manchester, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$15,429

9.0100, ENDOSSEOUS DENTAL IMPLANTS

C.L. Lavelle, University of Manitoba, School of Dentistry, Dept. of Oral Biology/Stomatology/Rehabilitative Dental Sci, *780 Bannatyne Ave., Winnipeg, Manitoba, Canada* R3E OW3

This study is based upon the fact that porous tricalcium phosphate ceramic may be resorbed and replaced by bone. Thus using this material to coat titanium posts, endosseous dental implants may be inserted into cavities in alveolar bone of analogous dimensions. Such alveolar cavities are produced atraumatically by a special water-cooled cutting device. After insertion, the implant is maintained stress-free until there is radiographic evidence of mechanical union between implant and alveolar bone with no intervening layer of connective tissue. Subsequently a conical epimobile polysulfone cone is attached to the implant in order to compensate, to a certain extent, for the lack of a periodontal ligament. This structure then serves for the attachment of crowns or bridge abutments. Preliminary investigations indicate that such a technique offers considerable potential, although there is yet scant evidence of the long-term prognosis of such devices.

SUPPORTED BY

University of Manitoba	funds n.a.

DIAGNOSIS & TREATMENT - GENERAL STUDIES

9.0101, BIODEGRADABLE MATERIALS FOR THE TREATMENT OF FRACTURES AND SOFT TISSUE WOUNDS IN THE MILITARY SITUATION

D.E. Cutright, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Surgery, *Washington, District of Columbia* 20012 (DA0K6020)

To determine the best usage of biodegradable copolymer materials for the treatment of both hard and soft tissue wounds. To develop premedicated biodegradable tissue fixation devices. To determine feasibility of a long-term, subcutaneous, slow release drug delivery system.

The recent adaptation by USAIDR of the biodegradable copolymers to the surgical procedures such as tendon gliding devices, oral antral fistula closure and peripheral nerve repair will be expanded in animals and extended to man. Application to the drug review board has been made for this usage.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research	funds n.a.

9.0102, POLYMERIZATION OF TOOTH RESTORATIVE COMPOSITE MATERIALS

D.T. Turner, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Operative Dentistry, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130150)

The objective of the research is to gain control of polymerization reactions used in dentistry to give optimal clinical performance. The methods of initiation studied include thermal decomposition of benzoyl peroxide which, because of its relative simplicity, provides insight into the mechanism of autoacceleration of polymerization. Redox systems are studied because of their importance in cold-cure systems and particular emphasis is being placed on the formulation of systems with long shelf life. Initiation by ultraviolet light is being studied in relation to its use for curing tooth restorative composite materials. major objective in this latter work is to determine the depth and lateral spread of photopolymerization.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$37,515

9.0103, STANDARD TEST METHODS FOR BIOMATERIALS & INSTRUMENTATION

J.W. Stanford, American Dental Assn., *211 E. Chicago Ave., Chicago, Illinois* 60611 (R01 DE 03505-10S1)

Emphasis will be placed on the clinical relevance and significance of various requirements and test methods in ANSI, ADA, FDA and ISO specifications. Comprehensive evaluations of methods for determining corrosion characteristics and physical properties of different alloys and products in dentistry will continue. These will include: conventional and high copper dental amalgams, low-gold, silver-palladium, non-precious and ceramic dental alloys. Characterization of the thermal expansion behavior of non-precious and procelain fused to metal alloys and porcelains will be done in addition to continued work with dental investments. Modification and improvement of thermal expansion measurement methods for dental investments will be investigated. Evaluation of proposed test methods for burs and diamond rotary cutting instruments will continue. Evaluation will be made of test methods for endodontic rasps, hedstrom files, and barbed broaches. Work on color stability test methodology and opacity standards development will continue.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$49,947

9.0104, NORMAL & ABNORMAL CELL ADHESION TO INANIMATE MATERIALS

R.D. Fletcher, University of Pittsburgh, School of Dental Medicine, Dept. of Microbiology, *C336 Salk Hall, Pittsburgh, Pennsylvania* 15213 (R01 DE 03983-04)

A new technique has been described for measuring the adhesive strength of a gingival cell line to an agar substratum by the modification of the original 'blister' test for adhesives. A cell monolayer was developed on a Petri dish with a hole in the center of the growing surface, overlayed with agar, and the system pressurized to debond the cells from the agar surface. Pressure changes were measured by a capacitance pressure transducer the output of which was measured by a strip-chart recorder. The modulus (E) of the agar overlay was determined and used in the calculation of the adhesive-bond strength (gamma a). The gamma a yield for the gingival cell line (cell-agar debond) was 48.8 ergs per cm2, and for the control (no cells) (agar-polystyrene debond) was 30.0 ergs per square cm. This technique is being utilized to tabulate the adhesion of various cells to an agar overlay medium. In addition, selected cells are being studied for their binding ability to any inanimate substratum. This latter technique for cell-rigid substratum adhesion measurements will allow the testing of any nontoxic inanimate material.

BIBLIOGRAPHIC REFERENCES: Fletcher, R.D., Shoemaker, R. and Albertson, Jr. J.N., 1977. Desmosomes Observed in a Gingival Cell Line. J. Dent. Res. 56:1106. Fletcher, R.D., Adamiak, J.K., Labant, M.C., Breitling, S.M., Williams Jr., M.L. and Albertson, J.N., 1978. Selected Physical Parameters Affecting Epithelial Cell-Agar Substratum Adhesion, in press.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

9.0105, DENTAL CARE OF THE CEREBRAL PALSIED CHILD

F.A. Harris, University of Washington, School of Medicine, Dept. of Physiology & Biophysics, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (R01 DE 04179-04)

The objective of this project is to facilitate the delivery of dental care to children who are handicapped by cerebral palsy. The constant, uncontrolled head movements typical of these children necessitate the use of general anesthesia in current practice to obtain safe, reliable access to the oral cavity. Our intent is to eliminate the 'involuntary' head movements through development of a device which will stabilize the patient's head in position desired by the dentist or hygienist. Development of the Head Stabilizer will be a multidisciplinary project involving biomedical sciences and engineering. The design of the device is such that the operator selects the desired head position using a joystick manipulator. Any time the desired and actual positions tend to differ, the resulting error signal leads to actuation of pneumatic cylinders which apply counteracting forces sufficient to return the head to the initially set point. The Stabilizer will first be tested with CP children to determine its efficacy and the time required for the children to become accustomed to it. Quantitative studies of head position under the influence of the Stabilizer will be carried out, and the effectiveness of the device will also be documented using cinematography. Next, dental procedures will be simulated to determine if the device can maintain head position despite these procedures. Dental hygienists, dental students and participating dental faculty will provide input regarding design optimization and development of accessories. Finally, the Stabilizer will be tested during actual dental procedures. Also, longer-term studies will be done to determine if it can be used to train CP children for improved voluntary head control through automatic provision of resistive exercise. After design optimization of the device, a CP dental care facility will be set up within the University of Washington School of Dentistry, where UW students and community dentists will be trained to use the device. An existing device which can be used to train CP children to brush their teeth will also be incorporated into the program to provide for dental maintenance.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $35,600

9.0106, THE DEVELOPMENT OF A DENTAL X-RAY AIMING DEVICE

J.I. Kaplan, Indianapolis Center for Advanced Research Inc., *1219 W. Michigan St., Indianapolis, Indiana* 46202 (R01 DE 04783-03)

The objective of this program is to design, fabricate, optimize, and use test and aiming device (which will determine the direction of the dental x-ray beam relative to the x-ray film in place in the patient's mouth) which will be located on the core of a conventional x-ray machine. Alignment will allow for the x-ray beam to be collimated to the appropriate film size. The aiming is accomplished via a pencil eraser sized permanent magnet located behind the film and two sets of three Hall effect probes located on the x-ray core. Equalization of the voltage read out from the Hall probes locates the x-ray axis. The indication for this will be a visual (and possibly an additional aural signal) display seen by the operator on moving the x-ray apparatus. The second year program will be primarily an optimization of the device and a cost reduction analysis and the third year will be primarily field testing of five units to be built at the end of the second program year.

SUPPORTED BY
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $18,119

9.0107, 10TH ANNUAL INTERNATIONAL BIOMATERIALS SYMPOSIUM

C.W. Hall, Southwest Research Inst., *8500 Culebra Rd., P.O. Drawer 28510, San Antonio, Texas* 78228 (R13 DE 05004-01)

This proposal is requesting funds to help support the planning and execution of the 10th Annual International Biomaterials Symposium to be held in San Antonio, Texas, at the Palacio del Rio, April 28-May 2, 1978. The conference will be directed toward bringing together clinicians, scientists, students and manufacturers for the purpose of exchanging ideas, information and to assess developments in the use of materials for implantation and reconstruction in the fields of dentistry, orthopedics, plastic, cardiovascular and general surgery. The first conference was organized and held on the Clemson University campus in 1969. In 1975, the Society for Biomaterials was formed and its first annual meeting was held in conjunction with the 7th International Biomaterials Symposium. In 1976 the conference started rotation and had its first off-campus symposium in Philadelphia. In 1977 the conference was held in New Orleans, and a return to the Clemson campus is being planned for 1979. Deviating slightly from previous protocol, this conference will, for the first time, include postgraduate instructional courses in the hopes that those who have entered the Biomaterials field from the clinical side can enjoy some instruction in Basic Engineering Language. Likewise, those entering from the engineering side can have the opportunity to have basic lectures in the Dynamics of Healing. All will have the opportunity to obtain in-depth knowledge in the area of Toxicology of Implant Materials and be brought up to date in the field of Medical Device Regulatory Affairs. Following the plenary sessions, contributed papers will be given in parallel sessions grouped into the general topics of Dental Orthopedic, Cardiovascular and Plastic Surgery. Specific topics such as biodegradation, tissue mechanics and material testing will likewise be presented. Careful selection of all contributed papers will be undertaken by a blind review of abstracts by the Program Committee.

SUPPORTED BY
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research $0

9.0108, 11TH ANNUAL INTERNATIONAL BIOMATERIALS SYMPOSIUM-1979

F.W. Cooke, Clemson University, School of Engineering, Dept. of Interdisciplinary Studies, *Rhodes Research Bldg., Clemson, South Carolina* 29631 (R13 DE 05432-01)

The purpose of this application is to request funds in the amount of $8,500 to plan and execute the 11th International Biomaterials Symposium to be held at Clemson University, April 28 to May 1, 1979. This Symposium is generally regarded as the premiere meeting in the field of Biomaterials and typically involves some 120 technical presentations and an attendance of 350 including representatives from most of the countries of Western Europe, Japan, Australia, Canada, India, The Middle East, and some from Latin America. Of the preceding Symposia, NIDR has been a sponsor of six.

It has become the traditional purpose of this Symposium to bring together basic and clinical researchers dedicated to the development and use of materials for reconstructive surgery considered in the broadest sense. This includes oral, dental, orthopedic, maxilo-facial, plastic, prosthedontic, and cardiovascular surgery. Orthotic materials and tissue considered as a material are also included. The leading investigators in all areas of biomaterials research are invited to submit papers on their current studies in the areas of: (a) the development and evaluation of materials for use in the body, b) the reaction of the living system to such materials, c) the design and development of improved prosthetic and orthotic devices based on these materials, d) and finally, the results of clinical experience with these materials and devices.

In all cases, emphasis is placed on the overall medical relevance and interdisciplinary communication.

As in past years, each day's program will begin with an invited plenary paper by an outstanding investigator in the relevant field. This will be followed by a series of submitted papers organized into thematic sessions. Besides the usual sessions in orthopedic, dental, prosthedontic, and cardiovascular materials, there will be sessions devoted to friction and wear, (probably 2 sessions), corrosion, percutaneous materials, wound healing, and infection in the presence of implants. The submitted papers will be chosen by blind review and all accepted papers will be collected in a printed Transactions volume.

The sponsorship of NIDR will be prominently acknowledged in the program and Transactions, and to all announcements in technical journals in the U.S. and abroad.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$8,500

9.0109, HARD COATING OF DENTAL ROTARY CUTTING INSTRUMENTS

B.K. Norling, University of Texas, Health Science Center at San Antonio, School of Dentistry, Dept. of Biomaterials, *San Antonio, Texas* 78284 (R23 DE 04407-03)

Commercial FG-57 dental carbide burs will be coated with several refractory intermetallic compounds (borides and carbides) by RF sputter deposition. The coated burs will be evaluated for any improvement in performance (initial cutting rate and durability) by means of a standardized milling test (300,000 rpm; 50, 100 and 150 gm load; 2 mm depth of cut; 1 cm cuts) using two work materials, a 50 percent diatomaceous earth-filled phenolic and soda-lime glass. Attempts will be made to delineate that combination of coating material, deposition parameters and thickness which provide optimal improvement in performance. Additional samples of burs from different manufacturers will be coated with the optimal coating to determine the effects of bur variability in carbide composition, flute design and edge sharpness on the (presumed) range of improvements to be obtained by hard coating.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

9.0110, DELAYED FAILURE AND AGING OF MELT-SPRAYED CERAMIC-METAL BONDS IN PHYSIOLOGICAL MEDIA

S.D. Brown, University of Illinois, Urbana Champaign Campus, School of Engineering, Dept. of Ceramic Engineering, *207 Engineering Hall, Urbana, Illinois* 61801 (DMR78-18084)

This biomaterials project will deal with delayed failure and aging of ceramic-metal bonds in physiological media. The objective will be to understand the mechanisms which underlie these processes, both in vitro and in vivo. Attention will be focused on the measurement of subcritical crack velocity in plasma-sprayed alumina-coated-metal systems. The effects of the character of the coating-substrate system and the composition of the physiological media on subcritical flaw propagation, aging and delayed failure will be ascertained. Stainless steel and a titanium alloy will be used as substrate materials, and the physiological media to be employed for in vitro experiments will include deionized water and various isotonic saline solutions. The results will be examined in terms of a multibarrier kinetics model of the subcritical crack velocity. Biocompatibility tests will be made in conjunction with in vivo aging experiments. These will involve evaluation of local changes in tissues surrounding the implants by examination of histological sections.

This is a continuation of NSF Grant DMR76-03893.

SUPPORTED BY

U.S. National Science Foundation, Directorate for Mathematical & Physical Sciences, Div. of Materials Research	$0

9.0111, THE AMOUNT OF WORK IN DENTAL TREATMENT - A LONGITUDINAL STUDY

R. Meeuwissen, Katholieke Universiteit Nijmegen, Dept. of Occlusal Reconstruction, *Erasmuslaan 4, Nijmegen, Netherlands*

What is the amount of work and dental skill per tooth invested in dental treatment? What is the lifetime of a tooth?

These questions will be answered by a retrospective longitudinal study of 500 patient records for a period of 20 years, 1957-1977. The patients concerned are 40-50 years old and are the members of the Royal Dutch Army and Air Force.

A pilot study validating the research instruments has been done.

We are putting forth the hypotheses that much more dental work is being done on the posterior teeth than on the anterior teeth. It is however a well known fact that the posterior teeth are lost first. If our hypothesis holds true this could imply a change in the philosophy of treatment for the future.

SUPPORTED BY

(No Supporting Organization Reported)	funds n.a.

9.0112, A STUDY OF THE NORMAL AND BEVELED CAVITY ANGLE WITH THE ELECTRON MICROSCOPE

E.J. Uribe, Universidad Nacional de Cordoba, Facultad de Odontologia, Catedre de Tecnica de Operatoria Dental, *5000 Cordoba, Argentina*

Divergent theories exist in dental literature concerning the drilled angle of the cavity wall at the periphery. This is especially true of beveled edges.

Using healthy upper and lower human premolars and molars extracted for othodontic reasons we prepared median-distal cuts with diamond disk high speed drills and obtained semi flat rough surfaces which were treated with an aluminum oxide rotary band of decreasing grain and lastly smoothed and polished with aluminum in water.

Above this we made half cavities using steel, carbon tungsten or diamond drills. The side of the cavities were beveled with distinct angles of depth and width and prepared for electron microscopy. (Translated)

SUPPORTED BY

(No Supporting Organization
Reported) funds n.a.

9.0113, HAZARDS TO FILLINGS FROM FLUOR-GEL APPLICATIONS

W.T. MacCulloch, National University of Ireland, University College at Cork, *Cork, Ireland*

It has been assessed that the caries incidence of those patients with few fillings declines or remains static when they are treated with fluorine-containing solutions which have been held in contact with their teeth by applicators.

However, because of the corrosion of metal fillings and the attack of quartz-containing silicate and composite fillings, it is estimated that the probability of replacement of such restorations will be increased in patients with multiple fillings.

The above contention is being investigated.

SUPPORTED BY

National University of Ireland funds n.a.

DIAGNOSIS & TREATMENT - ENDODONTICS

9.0114, DEVELOPMENT OF ENDODONTIC PROCEDURES FOR MILITARY DENTISTRY

J.M. Brady, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Basic Sciences, *Washington, District of Columbia* 20012 (DA0H6038)

Army endodontic procedures in the military total 108,000 per year and are 25 percent of dental emergency procedures. Tooth reimplantation with endodontic therapy is involved in most serious facial injuries and involves typically 3 to 5 patient visits. The military can gain at least a 50 percent reduction in patient and specialist man-hours spent in endodontic therapy with the development of more rapid and reliable treatment materials and techniques.

Two areas to be investigated under this project are- (1) analysis of endodontic materials including those in use and newly developed- (2) techniques used in endodontic therapy with emphasis on the development of the most rapid and accurate method within the military type practice.

SUPPORTED BY

U.S. Dept. of Defense, Army,
Medical Research &
Development Command, Inst.
of Dental Research funds n.a.

9.0115, DIFFERENTIATION OF ODONTOBLASTS IN PULPAL HEALING

W.A. Miller, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (R01 DE 04048-04)

The differentiation of pulpal cells into ondotoblasts during pulpal healing will be studied in two model systems with a view to developing biological method of pulp capping; i.e. in vitro models using enzymatically separated bovine pulp cells grown in monolayer initially and subsequently in a three dimensional cell culture system. Cells from various concentric regions of the bovine pulp will be stimulated to differentiate into preodontoblasts of odontoblasts and possibly form predentine and dentine. Stimulation will be by biological 'materials' such as dentine, predentine, enamel, reduced enamel epithelium, and root sheath. Cells will be cultured against several inert surface variables: Millipore filter (0.45 um and 0.1 um, both sides of the filter), cellophane, Teflon, isobutyl cyanoacrylate, and paper. The surfaces will be modified as appropriate. The commonly used endodontic materials, suitably modified for in vitro experiments will also be investigated. Enzyme biochemistry and histochemistry as well as transmission electron microscope techniques will be used to follow the interactions and differentiation of the cells involved.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $67,201

IX. RESTORATIVE MATERIALS & PROSTHESES

9.0116, BIOCOMPATIBILITY OF ENDODONTIC MATERIALS

K. Langeland, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Endodontics, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 04096-03)

The purpose of this investigation is to develop test methodology for evaluation of the biologic properties of endodontic materials with the long-range goal of suggesting biologic standards and specifications in accordance with the Medical Device Bill passed by the Congress 28 May 1976. Presently, the only tests which come near to expressing the true tissue reactions to the materials under usage conditions are the expensive and cumbersome experimentations in primates or the 'trial and error' in human patients - which should be avoided because it in fact involves human experimentation. It is proposed to investigate whether or not a correlation exists between specific primary screening tests and usage tests with the future aim of replacing the expensive usage tests with adequate, reliable, and relevant screening methods which will reduce the cost of testing while securing biologically safe materials to the patient. The proposed experimental systems and techniques for the correlation study are the following: (1) HeLa cells and human fibroblasts in tissue culture utilizing 51Cr release to measure cytotoxicity. (2) Assessment of enhanced vascular permeability and cellular response in connective tissue in rats after intradermal injection of the material. (3) Evaluation of response to implants in soft tissues and bone tissues in guinea pigs. (4) Evaluation of inflammatory response in remaining pulp tissue and in periapical tissue of monkeys. The methods of evaluation include radio-isotope measurement, SEM, and electron probe, and histopathological techniques. The correlation of these tests will provide economical and relevant screening methods which may be used by manufacturers during their development of new products and for their quality control. Ultimately, it secures biologically safe materials to the patient population, and eliminates inefficient and/or toxic materials from use.

BIBLIOGRAPHIC REFERENCES: Macko, D.J., Rutberg, M., and Langeland, K.: Pulpal response to the application of phospheric acid to dentin. Oral Surg., 45:930-946, 1978. Wyman, T.P., Dowden, W.E., and Langeland, K.: Staphylococcus aureus isolation from a clinically non-exposed root canal. J. of Endod., 4:122-128, 1978.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $68,141

9.0117, IMPROVEMENT IN CHARACTERISTICS AND USE OF GUTTA-PERCHA

S. Oliet, University of Pennsylvania, School of Dental Medicine, Dept. of Oral Medicine, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (R01 DE 04206-03)

Overall objective of this project is the standardization and improvement in the use of gutta-percha based materials for filling root canals. Characterization of the aging process by chemical changes and the determination of the effect of aging on mechanical properties will be continued. Investigation will also be conducted to determine thermal conductivity and melt-flow characteristics utilizing simulated and actual root canals. Determination will be made of optimum cone composition and characteristics as well as appropriate test equipment for inclusion in specifications. Recommendations will be made for improvement of clinical procedures.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

9.0118, REVITALIZING PULPLESS TEETH USING COLLAGEN-CAPO4 GEL

A.J. Nevins, Nassau County Medical Center, Dept. of Dentistry, *2201 Hempstead Tpke., East Meadow, New York* 11554 (R23 DE 04552-03)

Previous studies have shown that a gel composed a calf skin collagen, CaC12 and K2HPO4 can induce hard connective tissue into pulpless open apex teeth in Rhesus monkeys. The purpose of this study was to determine if this gel, cross-linked in glutaraldehyde, would support connective tissue growth into debrided root canals.

Thirty maxillary and mandibular incisor teeth, 20 partial pulpectomies and 10 total pulpectomies were done in incisors of 6 Rhesus monkeys. One half of each procedural group was filled with collagen-calcium phosphate gel and one half a CaOH-saline paste to serve as controls. Animals were killed at time periods ranging from 3 to 8 months. Block sections of bone containing the teeth were removed and prepared for histologic examination.

Sections showed hard tissue forming within root canals of 13 teeth filled with collagen-mineral gel. Nine of 15 control teeth resulted in hard tissue formation adjacent to the CaOH-saline paste.

Collagen-CaPO4 gel cross-linked with glutaraldehyde appears to induce more complete regeneration of connective tissue within debrided root canals than CaOH-saline paste.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

9.0119, COMBINED DENTAL RESEARCH PROGRAM - PERIODONTICS SECTION - ENDODONTIC SECTION

W.C. Bird, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Periodontics Section, *1201 Broad Rock Rd., Richmond, Virginia* 23249 (652-001-P)

For summary: see 2.0282.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

DIAGNOSIS & TREATMENT - TRANSPLANTS/REPLANTS

9.0120, ROOT FORMATION IN LOWER VERTEBRATE TOOTH TRANSPLANTS

R.I. Howes, University of Oklahoma, Health Science Center, School of Medicine, Dept. of Anatomical Sciences, *Box 26901, Oklahoma City, Oklahoma* 73190 (R01 DE 03709-06)

The past periods of this tooth transplant research enabled me to examine experimentally tooth and root formation in autogenous transplants of a fibrous, hinged, ankylosed, or socket type of tooth attachment. The current and future direction of this project is to place emphasis on the more successful animal models. Since teeth migrating into a regenerating wound area of the jaw develop in a similar manner to those buds which are transplanted ectopically, work is to proceed on both areas of tooth growth and the tissues which comprise their environment. A major task will be examination of mostly anorganic preparations of normal and transplanted teeth, roots, and jaws with the scanning electron microscope (SEM). Normal teeth have at least five distinguishable surface areas in anorganic preparations. This number and appearance varies with the age of the adult tooth. The surrounding mucosa of the healing jaw wound will also be examined using the SEM. In addition to specific long-term transplant studies using successful models, the behavior and fate of tooth buds growing within the tail musculature of the catfish will be studied. Preliminary findings show enhanced growth at that site including growth of the bony portion of the tooth attachment. Finally, growth of regenerating teeth taken from jaw wounds and transplanted into the anterior chamber of the eye will be examined along with initial experiments of transmission electron microscopy of the epithelial covering of the root surface of the frog. It is hoped that more will be learned about the nature of the tooth attachment, the process of oral healing, and the relation of the tooth number and dental lamina morphology to success in tooth and jaw regeneration.

BIBLIOGRAPHIC REFERENCES: Howes, R.I. 1978 Root formation in ectopically transplanted teeth of the frog. Rana pipiens: Part 11, Comparative aspects. Acta Anatomica 100: 461-470. Howes, R.I. 1978 Regeneration in ankylosed teeth in the premaxilla of Rana pipiens. Acta Anatomic 101:179-186.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$18,608

9.0121, TOOTH TRANSPLANTATION GENETICS AND IMMUNOLOGY

G.R. Riviere, University of California, Los Angeles Campus, School of Dentistry, Dental Research Institute, *405 Hilgard Ave., Los Angeles, California* 90024 (R01 DE 04489-04S1)

Teeth transplanted between mice that are matched for the major histocompatibility complex (MHC) but who differ by non-MHC antigens elicit immune responses that may promote their own survival. The purpose of this research is to identify the role played by cellular and/or humoral factors in the permanent survival of teeth transplanted between mice disparate for 1 or 2 non-MHC loci. In addition, we hope to demonstrate that teeth transplanted across a multiple non-MHC barrier elicit graft-protective immunity and that this immune state is associated with long term graft survival. Teeth will be transplanted to heterotopic and orthotopic sites in recipient mice who differ by 1, 2, or several non-H-2 antigens. Control animals will receive skin grafts or allotransplants of bone. Recipients will be studied for cellular and humoral cytotoxicity and for cell-mediated and antibody-mediated suppression of immunity in vitro and in vivo. Survival of tooth allografts will be confirmed by routine histological procedures.

IX. RESTORATIVE MATERIALS & PROSTHESES

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$53,136

9.0122, REVASCULARIZATION AND REATTACHMENT FOLLOWING TOOTH TRANSPLANTS

C.E. Nasjleti, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *2215 Fuller Rd., Ann Arbor, Michigan* 48105 (506-003-P)

This long-term investigation is progressing according to plans. As a by-product of this research, we recently reported: Revascularization of the periodontal membrane after tooth replantation in monkeys.

The abstract of the paper reads as follows: a total of 13 maxillary incisors replanted without root canal therapy were studied to evaluate the pattern of revascularization of the periodontal membrane and the modification of its vasculature due to root cementum resorption, dentoalveolar ankylosis, and periapical processess. The revascularization of the dental pulps was also evaluated. The replanted central incisors were splinted to the adjacent lateral incisors for one week. The animals, sacrificed at 4, 7, 15, 21, and 31 days, and 3 months, were perfused with India ink and buffered formalin solution. Blocks containing the replanted and lateral incisors were processed to obtain cleared specimens and serial histological sections.

RESULTS: Early reparative activity was noted in the apical and cervical parts of the replanted periodontal membrane where proliferation of vessels were disorderly arranged with reparative cells and new collagen. These areas of the membrane were identificable with those receiving better vascular supply after replantation. The mid-third of the membrane, however, showed scarcity or absence of reparative cells due to delayed revascularization. In those cases of root cementum resorption, dentoalveolar ankylosis or periapical processes, there was close adaptation of the local vasculature to the tissue specificity of those conditions. Revascularization of the pulp tissue was successful in one specimen (4-days); all other pulps showed vacuolar degeneration due to lack of vascular supply.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

PREVENTION

9.0123, CLINICAL VERIFICATION OF FISSURE SEALANTS

J.J. Cuello, Universidad Nacional de Cordoba, Facultad de Odontologia, Catedra de Clinica de Operatoria Dental, *5000 Cordoba, Argentina*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

(No Supporting Organization Reported)	funds n.a.

9.0124, A 5-YEAR EVALUATION OF FISSURE SEALING OF THE TEETH OF MENTALLY RETARDED CHILDREN

B.A. Richardson, University of Toronto, School of Dentistry, *124 Edward St., Toronto, Ontario, Canada* M5G 1G6

PURPOSE: To evaluate fissure sealing as a preventive dental technique with special emphasis on the problems of mentally retarded children.

SUBJECTS: 160 mentally retarded children (64 percent male, 36 percent female), ages 5 to 21, IQs 30 to 80, selected from residents of the Midwestern Regional Children's Centre, Palmerston, Ontario.

METHODS: The study consists of clinical dental examinations at 3-month intervals of the children who participated in the initial study. Recordings of the incidence of decayed, missing, and filled teeth are made for both the teeth treated with sealant and the untreated control teeth. The examination is made independently by two assessors who were involved in the initial trial. The statistical methodology developed by Cvar (test of significance, percent effectiveness, and net gain) will be used to evaluate the results and to ascertain if there is a long-term benefit from a single application of a resin fissure sealant to the teeth of these children.

FINDINGS: At the end of the 1st year, 136 children were examined and a total of 665 teeth were evaluated: 72.2 percent of these teeth remained sealed and 2.2 percent were extracted or exfoliated. At the end of the 2nd year, 144 children were examined and a total of 686 teeth were evaluated: 59.5 percent of these teeth remained sealed and 19.2 percent partially sealed; 18.1 percent were not sealed, 3.2 percent were extracted or exfoliated. The percent effectiveness had decreased from 78.8 percent the 1st year to 67.9 percent the 2nd year. The results of both years were highly significant. Although the percent effectiveness had decreased nearly 11 percentage points, from the 1st to the 2nd year, the sealant still is significantly effective. It seems desirable, on preventive and sociological grounds, that mentally retarded children should have their teeth treated by such sealant procedures.

SUPPORTED BY
(No Supporting Organization
Reported) funds n.a.

X. PAIN CONTROL & BEHAVIORAL STUDIES

EPIDEMIOLOGY

10.0001, SECOND WORLD CONGRESS ON PAIN

J.J. Bonica, International Assn. for the Study of Pain, *21 Dupont Cir. N.W., Washington, District of Columbia* 20036 (R13 DE 04368-02)

The Second Wrold Congress on Pain, sponsored by the International Association for the Study of Pain, will be held in Montreal, Canada on August 27 to September 1, 1978. Like the First World Congress which was held in Florence, Italy on September 5-8, 1975, the goals and objectives of the Congress are to bring together scientists, physicians, and other health professionals from various parts of the world and representing virtually every basic science and clinical discipline to report new information and reappraise current knowledge on pain mechanisms and various therapeutic modalities in current use. The scientific program of the Congress will include 5 plenary (single track) sessions, free communications, and other activities as described in the proposal.

The plenary session and the free communications on Orofacial Pain will constitute approximately 25 percent of the scientific program of the Congress. In addition, a special satellite meeting on Orofacial Pain will be held prior to the Montreal Congress on August 25-26. 1978, in Toronto, Canada. In these two meetings it is planned to discuss virtually every aspect of orofacial pain.

Based on the experiences of the First World Congress, it is anticipated that: (1) Over 1,000 biomedical scientists and health professionals, representing every basic science and clinical discipline from over half the countries in the world will attend the Second World Congress; (2) About 350-400 presentations will be made; (3) The Congress will enhance interaction, communication, and cross-fertilization among the participants of different disciplines; (4) It will greatly facilitate the rapid application of new knowledge to the diagnosis and treatment of acute and chronic pain, including that in the mouth and face. Moreover, the Congress should help define more clearly the needs and direction of future research efforts and provide opportunities for collaborative interdisciplinary study and treatment of orofacial pain. The ultimate goal is to help improve the care of patients with acute and chronic pain, which currently constitute a major national and world health and economic problem.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

ETIOLOGY - BASIC NEUROPHYSIOLOGY, ANATOMY, & BIOCHEMISTRY

10.0002, CEREBRAL RESPONSE TO TOOTH PULP STIMULATION (HUMAN)

G.E. Chatrian, University of Washington, School of Medicine, Dept. of Laboratory Medicine/Neurological Surgery, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (M01 RR 00037-190212)

This project is part of a broader program (RR 00037-19) whose summary states: The Clinical Research Center at the University Hospital was activated in 1960 and has been maintained through support by the National Institutes of Health. This multidisciplinary facility provides a milieu for the conducting of clinical research encompassing a broad spectrum of human physiopathology and disease. The specific purposes are to provide an environment for investigation of human physiology in health and disease under carefully monitored conditions and to provide optimal medical supervision and protection of the human subjects' rights and welfare. This facility also enables the study of unusual diseases or unique opportunities to study commonly encountered clinical disorders under conditions or supervision which could not be readily obtained in primary clinical care facilities. The Center also constitutes a place where postgraduate and undergraduate students in medicine, nursing, and diabetics can obtain in-service experience in clinical research under established investigators.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health, Div. of
Research Resources funds n.a.

10.0003, NEAR AND FAR FIELD EVOKED POTENTIALS AND PAIN REACTIVITY

W.K. Dong, University of Washington, School of Medicine, Dept. of Anesthesiology, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (P01 DE 05130-010005)

We propose to identify cortical and brainstem sites that mediate and process nociceptive trigeminal/dental input as well as to determine the relative contribution of these sites to 'pain' behavior in the cat and monkey. The lemniscal and extralemniscal components of 'dental' near and far-field potentials will be identified by selective lesions of cortical and brainstem sites in acutely and chronically prepared animals. Moreover, the effects of selective cortical and brainstem lesions on the threshold, latency and force of escape responses evoked by dental stimulation will be assessed. Our experimental design allows detailed contrast of changes in near and far-field responses to noxious dental stimulation with assessment of behavioral response within the same animal at the same points in time. Hence we will be able to identify at several levels of the central nervous system those sites that underlie transmission and processing of signals resulting from noxious dental stimulation. These sites may constitute collectively an important part of the underlying basis for sensation and behavioral manifestations of orofacial pain.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $119,883

10.0004, CORTICAL PROJECTIONS OF THE VENTROPOSTERIOR AND SURROUNDING THALAMIC NUCLEI

B.L. Whitsel, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Physiology, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130198)

This project seeks to determine the organization of the thalamic projections to the somatic sensory cerebral cortex (areas S-I and S-II) in monkeys. A combination of neuroanatomical tracing procedures and single neuron recording techniques is used to identify the thalamic neurons projecting to cortical zones containing neurons with known functional characteristics. The data are anticipated to extend current views of the functional architecture of the primate somatic sensory cerebral cortex.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $18,149

10.0005, NEURAL MECHANISMS OF THE DIRECTIONAL SELECTIVITY DISPLAYED BY SOMATOSENSORY CORTICAL NEURONS

B.L. Whitsel, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Physiology, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130199)

The objective of this project is to identify by means of intracellular recordings the mechanisms that enable certain cerebral cortical neurons to respond differentially to stimuli that move in different directions over the same region of skin. Intracellular injections of horseradish peroxidase will be used to identify the morphology of the populations of somatosensory critical neurons which are distinguishable on the basis of their response to moving tactile stimuli.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $10,551

10.0006, STATISTICAL ANALYSIS OF THE SPIKE TRAINS EMITTED FROM SOMATOSENSORY NEURONS DURING CONSTANT VELOCITY STIMULATION OF THE SKIN

B.L. Whitsel, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Physiology, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130200)

The objective of this project is to determine the influence of the random element in neuronal discharge on the coding of tactile stimuli by individual somatosensory neurons. The data will serve as a basis for (1) identifying the neural mechanisms underlying the effects of centrally acting drugs on human somesthetic capacities, and (2) interpreting the effects on somesthetic behavior of lesions placed within one or another of the principle somatosensory projection pathways.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $13,506

10.0007, STUDIES OF MAXILLOFACIAL PAIN MECHANISMS AND CONTROL - NEUROSENSORY STUDIES OF POST-TRAUMATIC TRIGEMINAL NEURALGIA

J.M. Gregg, University of North Carolina, Chapel Hill Campus, Dental Research Center, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130202)

A computer-assisted model for quantifying the severity of chronic clinical pain problems has been developed. It is used as a basis for diagnostic input by members of a multidisciplinary team and also to serve as a more objective basis for studies of pain mechanisms and potential therapies. The objectives of this phase of the overall project are to characterize the neurosensory status of patients who have sustained trigeminal nerve injury and to relate these findings to post-traumatic pain syndromes. A six step analysis protocol will be followed including: 1) a demographic 'pain profile' survey, 2) a battery of classical neurosensory threshold tests, 3) thermographic studies of neurotrophic effects, 4) tactile and thermal signal detection psychophysics, 5) pain and sensory responses to nerve blocks with graded local anesthetic concentrations, 6) pain and sensory responses to topical norepinephrine and stellate ganglion sympathetic block. These studies are applied retrospectively to patients with chronic painful injuries and also prospectively to patients facing elective surgery with a likelihood of iatrogenic injury. It is hoped that this research will both clarify pain mechanisms in post-traumatic neuralgia and also set guidelines for more effective therapy.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $28,223

10.0008, STUDIES OF MAXILLOFACIAL PAIN MECHANISMS AND CONTROL - METABOLIC FACTORS IN CHRONIC PAIN

J.M. Gregg, University of North Carolina, Chapel Hill Campus, Dental Research Center, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130203)

A computer-assisted model for quantifying the severity of chronic clinical pain problems has been developed. It is used as a basis for diagnostic input by members of a multidisciplinary team and also to serve as a more objective basis for studies of pain mechanisms and potential therapies. The long range goal of this phase of the overall project is to determine the role of certain biochemical factors in the pathophysiology of chronic musculoskeletal pain and to measure these factor responses among patients receiving two experimental types of therapy. Comparisons will be made in plasma concentrations of serotonin, cortisol, and endorphins among subjects with no pain, acute post-surgical pain and chronic musculoskeletal pain in the maxillofacial region. With this protocol as a background a second phase study will be made of the possible analgesic effects of calcitonin. Support studies of laboratory animal noxious responses will parallel the human studies in which TC will be given with cross-over placebo to subjects with experimental pain, pain of Paget's disease of bone, and head and neck myofascial pain. In a final phase study, the previously mentioned biochemical factors will be assessed along with therapeutic responses among patients with chronic pain who are to be treated by aerobic exercise training.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $28,223

10.0009, RESPONSES TO TOOTH PULP STIMULATION IN HUMANS

G.E. Chatrian, University of Washington, School of Medicine, Dept. of Laboratory Medicine, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (R01 DE 03485-06)

We propose to continue and expand our investigations of computer-summated cerebral potentials elicited in human subjects by discrete electrical stimuli delivered to the pulp of individual teeth via electrodes implanted into dentine. This research will include: an investigation of the pre-pain range of stimulus intensities and qualities of pre-pain sensations with electrical tooth pulp stimulation; a study of the relationships among intensities of electrical stimulus to tooth pulp, subjective estimates of the effects of analgesic drugs on cerebral tooth pulp evoked potentials and subjective estimates of magnitude and quality of sensations in humans.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $56,536

10.0010, RECEPTOR FUNCTION AND RELATED STUDIES IN ORAL BIOLOGY

G. Mooser, University of Southern California, School of Dentistry, Dept. of Biochemistry, *3551 University Ave., Los Angeles, California* 90007 (R01 DE 03739-07)

Glycosyltransferases from oral bacteria are being studied. Of particular interest are the kinetic mechanism, physical characteristics of the purified protein and effects of protein modification reagents on dextransucrase from Streptococcus mutans.

BIBLIOGRAPHIC REFERENCES: Mooser, G. and N. Lambuth (1977) Inactivation of Taste

Receptor Cell Function by Two Cationic Protein Modification Reagents. J. Neurobiol. 8:193-206.

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National Inst. of Health,
National Inst. of Dental
Research $82,929

10.0011, QUANTITATIONS OF HUMAN PULP INNERVATION

D.C. Johnson, West Virginia University, School of Dentistry, Dept. of Pediatric Dentistry, *Morgantown, West Virginia* 26506 (R01 DE 04091-03A1)

Pain sensitivity of permanent teeth at various stages of development is of clinical concern. The dentist's perception of a tooth's pain sensitivity may influence his treatment. If differences in sensitivity normally exist at different stages of tooth development the dentist should understand these differences and the factors responsible.

The first part of the proposed project will provide new information on innervation levels for human teeth at various stages of development, as well as additional information on sensitivity. The parameters to be determined and correlated are: the number of myelinated and unmyyelinated sensitivity of a tooth as determined by electron microscopy, the threshold sensitivity of a tooth as determined by electrical stimulation, the stage of changes and arrangement of intrapulpal nerve fibers with progressive stages of tooth development and aging will also be described. Stage of tooth development will be determined by the degree of root formation in teeth erupted less than five years and by subject age when teeth have been present more than five years. Clinically healthy (no carious lesions; at least half of the bony support; no abrasion and only normal amounts of attrition) mandibular first premolars from humans will be studied at three stages of development: 20 premolars erupted less than five years at various stages of root development; 15 premolars erupted less than five years at various stages of root development; 15 premolars erupted approximately 10 years; 15 premolars erupted approximately 25 years.

Pulpal effects with orthodontic treatment are not reported in any detail. The second part of the project will examine the effect of orthodontic tooth movement on intrapulpal nerve fibers. Using as controls appropriate teeth from the first part of the study, ten premolars will be examined in this part. Numbers of nerve fibers will be determined as well as the percentage which display morphologic changes. Sensitivity tests will be done before tooth movement and prior to extraction. Five teeth will be examined after short periods of movement (less than 10 days) and five at longer periods (1-2 months).

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $20,358

10.0012, FACIAL AFFERENTS WITH PARTICULAR REFERENCE TO PAIN

L.L. Furstman, University of California, Los Angeles Campus, School of Dentistry, Dept. of Orthodontics, *405 Hilgard Ave., Los Angeles, California* 90024 (R01 DE 04249-03)

This proposal deals with the development of light microscopic neuroanatomical techniques which can ultimately be integrated into neurophysiological and ultrastructural studies of afferent central nervous system connections from the orofacial area. The proposed experiments will utilize horseradish peroxidase histochemistry as a dental research tool. Recent work in this laboratory has shown that this enzyme has been picked up by sensory receptors of the orofacial area and carried via retrograde axonal transport to the trigeminal complex in the brain stem. Studies are described which should make this method: 1) applicable to the morphological analysis of sensory nerve endings of the dental pulp and the temporomandibular joint and the localizations of their terminals, 2) useable in determining the rate and distribution of protein, 3) applicable for the identification of specificity of central organization in terms of modalities of sensory input, and 4) applicable to the analysis of sensory nerve endings of any orofacial area and the localization of their terminals.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

10.0013, PHYSIOLOGICAL BASIS OF DENTAL ELECTRICAL PAIN THERAPY

P.J. Reynolds, Oregon State Higher Education System, University of Oregon Health Sciences Center, School of Dentistry, Child Study Clinic, *611 S.W. Campus Dr., Portland, Oregon* 97201 (R01 DE 04281-03)

The therapeutic application of electrical current enjoys widespread use in dentistry, involving the procedures of vitalometry, electroanalgesia, and desensitization. The procedures are generally considered harmless, but our data and calculations indicate a high probability of damage and destruction in many typical situations. The present work is directed to an identification of electrical waveforms suitable for optimal therapeutic effects with minimal contingencies.

The primary objective of these experiments is to characterize the acute and chronic effects of simulated electrotherapeutic stimulation in the experimental animal, including several untested, more desirable waveforms. Three independent categories of data will be collected to characterize, respectively, pulpal nervous excitability (electrophysiology), tissue morphological alterations (histopathology), and alterations in key cellular metabolites directly related to nervous excitability and general metabolic integrity (biochemical energy-charge characterizations of pulpal ATP systems). The neurophysiological studies will involve standard single-unit electrophysiological recording techniques in the Gasserian ganglion both during simulated electrotherapeutic stimulation and following acute post-stimulus intervals of several hours. The histopathological and biochemical characterizations are to be conducted on material sampled after various chronic post-stimulus intervals of particular clinical interest, accompanied of necessity by a less direct measure of excitability, the thresholds for the jaw-opening reflex.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

10.0014, STRUCTURE-FUNCTION CORRELATES OF INTRADENTAL NERVES

U.L. Karlsson, University of Iowa, School of Dentistry, Dept. of Pedodontics, *Jessup Hall, Iowa City, Iowa* 52240 (R01 DE 04339-02S1)

The morphological identity and organization of nerve receptors in teeth are sought through three-dimensional reconstruction techniques for transmission electron microscopy. The approach is to use feline mandibular canine teeth as a model and to compare normal specimens with those which have been selectively (trigeminal and sympathetic) or totally denervated. The aim for next year is to finalize the normal organization in terms of interrelationships between participating cells, i.e. nerves, odontoblasts and fibroblasts. Preliminary results indicate a high level of organization between these three cellular constituents which may be presumed to participate in the receptor.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $0

X. PAIN CONTROL & BEHAVIORAL STUDIES

10.0015, DENTAL AND OROFACIAL PAIN - BRAIN STEM MECHANISMS

B.J. Sessle, University of Toronto, School of Dentistry, Division of Biological Sciences, *124 Edward St., Toronto, Ontario, Canada* M5G 1G6 (R01 DE 04786-02)

We have been studying in cats the functional organization of trigeminal brain stem neurones activated in particular by noxious facial an tooth pulp stimuli, and the modulation of this activity by sensory impulses initiated by other orofacial stimuli (e.g., tactile) and by endogenous descending influences. We have found that many cells in nucleus caudalis, considered to be the most essential orofacial pain relay site in the brain stem, show various patterns of discharges evoked by stimulation of orofacial nociceptive afferents; some relay their information directly to thalamus. However, this relay can be suppressed by other orofacial stimuli and particularly by stimulation of periaqueductal gray and nucleus raphe magnus. These sites have recently been implicated in endogenous analgesic mechanisms partly related to the action of narcotics, acupuncture, etc., through the release of endogenous chemicals (e.g., enkephalin). We intend to study these mechanisms further; iontophoretic methods may be particularly worthwhile since we have already found in preliminary published studies that, in contrast to our observed excitatory action of substance P on nociceptive neurones, enkephalin and pain control drugs can suppress such neurones. We have preliminary published evidence that presynaptic regulatory mechanisms contribute to the observed suppressive influences on orofacial nociceptive transmission, and we intend to study these mechanisms further.

BIBLIOGRAPHIC REFERENCES: Sessle, B.J., Hu, J.W. and Lucier, G.E. Periaqueductal gray matter-induced suppression and naloxone reversal in trigeminal nociceptive neurones. Pain Abstracts 1: 74, 1978. Hu, J.W., Dostrovsky, J.O. and Sessle, B.J. Tooth pulp primary afferent depolarization (PAD) and naloxone: are presynaptic opiate receptors involved? Soc. Neurosci. Abstracts 4: 01462, 1978.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,

National Inst. of Dental
Research $50,313

10.0016, NEURAL PROCESSES IN SOMATIC MOVEMENT

E.S. Luschei, University of Washington, School of Medicine, Dept. of Physiology & Biophysics, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (R01 DE 04884-11)

Research is concerned with the neurophysiological mechanisms involved in voluntary and reflex control of jaw movements in intact, unanesthetized, animals. Monkeys are trained to control either incisal biting force or jaw position by having them observe a visual spatial representation of either of these variables and keep the visual feedback signal within a visual target zone. In some cases, sinusoidal perturbations of the load or position are imposed by a servo mechanism to study the reflex regulation of these variables. Activity of jaw muscle spindle afferents or neurons of the face area of the precentral cortex is studied in relationship to these behaviors. Selective lesions of these structures are produced to determine their contribution to the properties of jaw control. Neural recording and lesions in various structures of the brain of the guinea pig will be used to study the subcortical neural mechanisms involved in the production of jaw movement and muscle activity patterns associated with mastication.

BIBLIOGRAPHIC REFERENCES: Clark, R.W., E.S. Luschei, and D.S. Hoffman. Recruitment order, contractile characteristics, and firing patterns of motor units in the temporalis muscle of monkeys. Exptl. Neurol., 61, 31-52, 1978. Goodwin, G.M., D.S. Hoffman, and E.S. Luschei. The strength of the reflex response to sinusoidal stretch of monkey jaw closing muscles during voluntary contraction. J. Physiol., London, 279, 81-111, 1978.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $47,776

10.0017, TEETH AND TRIGEMINAL PATHWAYS

L.E. Westrum, University of Washington, School of Medicine, Dept. of Neurological Surgery/Biological Structure, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (R01 DE 04942-02)

The objectives of this project are to study the morphological effects of tooth pulp extirpation, extraction of teeth and exfoliation of deciduous teeth on the trigeminal system. Light and electron microscopical methods will be used to analyze and evaluate the sequence of acute and chronic alterations in the sensory neurons of the trigeminal ganglia, their central axons and synaptic endings in the main sensory and spinal trigeminal nuclei. Extirpation of tooth pulps and extraction of teeth will be performed on adult cats and a variety of short-term and long-term postoperative survival times will be studied. Young cats undergoing various stages of tooth replacement will be used to determine possible changes caused by exfoliation of deciduous teeth and eruption of permanent teeth upon neuronal structures of the trigeminal system. Retrograde nerve cell changes in the trigeminal ganglia will be correlated with the study of degeneration of their axons and synapses in the brain stem trigeminal nuclei. The type of cells and axons, the population and character of synapses and their distribution in the brain stem, the precise sequence and pattern of degeneration, the possible transneuronal effects and potential regenerative capabilities of these axons and synapses will be studied and characterized in each of the preparations. The project will be useful in providing new information about the anatomical representation for the teeth within the central nervous system and will also provide possible morphological explanations for certain sensory alterations, including pain-related symptoms, associated with dental surgery, endodontic therapy, tooth loss or trauma involving these structures.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $42,444

10.0018, ANATOMIC STUDY OF TRIGEMINAL PRIMARY AFFERENT FIBERS

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The current theories of the neurophysiological mechanisms of somatosensory perception emphasize the importance of cavity in primary afferent fibers of varying size and degree of myelination. In spite of studies performed over the last 75 years there is as yet no convincing analysis of the fiber size spectra and myelinated to unmyelinated ratios of afferent nerves. The impossibility of accurately measuring fiber in the 1-2 micron or less range using the light microscope is primarily responsible for this. Variations in fiber ratios have been proposed as the pathophysiological mechanism for such pathologic pain states for example as trigeminal neuralgia and post herpetic neuralgia. In addition while many physiological studies have attempted to locate the termination of primary afferent fibers related to pain perception at both the spinal cord and trigeminal levels no attempt at anatomic tracing has been carried out.

We propose to utilize electron microscopic analysis of the fiber spectra of the spinal and trigeminal roots of various species in an attempt to establish their fiber size spectra and myelinated to unmyelinated fiber ratios of these animals.

In addition we propose to trace the path and central termination of the fibers from the dental pulp, using electron microscopic radioautography.

We believe that the variations in fiber spectra and ratios may represent an individual species recapitulation of the phylogenetic process of encephalization. Further, tracer method will provide anatomic evidence of the termination of primary afferent fibers related to pain perception which can be interpreted in the light of various physiological theories.

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Services, Public Health Service,
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Research $0

10.0019, DISTRIBUTION AND ULTRASTRUCTURE OF DENTAL INNERVATION

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Sensory properties of teeth and periodontium are not well understood, both because of difficulties in dividing single-unit studies of dental tissue, and bacause of insufficient information of the distribution of trigeminal gasserian and mesencephalic nerve endings, the utlrastructure of these endings, and their relationship to autonomic nerves and to odontoblasts or periodontal cells. Recently, by using autoradiography to detect nerves labeled by radioactive axonal transport, we have demonstrated gasserian nerve endings in rats, and have described the ultrastructure of the dentinal and pulpal endings.

The proposed research will use similar methods to study dental innervation in monkeys and rats. The specific objectives are: (1) to map mesencephalic and autonomic nerve endings in rat and monkey teeth and periodontium: (2) to develop a procedure for labeling gasserian endings in monkeys and to map these endings in monkey molars, canines, incisors, and periodontium; (3) to compare the ultrastructure of labeled gasserian and mesencephalic endings using EM-autoradiography; (4) to determine the kinds of junctions formed by trigeminal or autonomic nerve endings and odontoblasts or periodontal cells; (5) to measure the sizes of axons derived from labelled gasserian, mesencephalic, or autonomic nerve endings; (6) to study innervation in extracted monkey teeth.

This research will contribute to our understanding of the cellular basis of dental pain and proprioception; to determination of the role of autonomic innervation in dental sensitivity; and to identification of the kinds of innervation that typify all mammalian teeth as opposed to innervation unique to particular species or types of teeth. The long-range goal is to correlate these studies with functional studies to provide greater insight into the mechanisms of dental sensitivity and pain.

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Research $77,003

10.0020, OPERANT NEURAL CONTROL IN TRIGEMINAL PAIN SYSTEMS

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The objectives of this proposal are: 1) Operant conditioning of amplitudes of evoked potentials in trigeminal nucleus, midbrain reticular nucleus intercolliclaris, thalamic ventro-basal complex and centremedian-parafasicularis complex, and cortical oro-facial areas in rats. (The potentials are evoked by pulses to the primary trigeminal tract.) 2) Study and comparison of analgesic effects of the 'neural biofeedback' in the loci just listed on oro-facial aversive reactions presumed related to trigeminal pain.

Rats will be rewarded when evoked potential amplitude is changed. Five kinds of oro-facial nociceptive reactions will be compared before and during asymptotic levels of conditioning.

This proposal may provide a clear demonstration of the functional significance of operant control of neural activity. This would be the first demonstration of such effects with evoked potentials, the conditioning of which has been demonstrated to be a non-trivially mediated, novel operant. The proposal aims at developing a new method of pain control with potential human clinical applications. The proposal to compare different conditioning effects in different brain loci may suggest differences in functional relevances of these loci for pain and analgesia. That is, control of some loci may produce analgesic effects, control of others may not. The former but not the latter loci would then appear to be connected to analgesia systems under conscious control.

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10.0021, MECHANISMS OF DENTAL AND FACIAL SENSATION

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The mechanisms which determine whether an orofacial stimulus is perceived as painful or innocuous are undetermined. Most investigators have felt that these two types of stimuli are qualitatively different but recently, it has been suggested that they may be only quantitatively different. Both ideas are based on the sensory changes which follow the surgical procedure of trigeminal tractotomy. Many physiological studies of orofacial sensation have employed dental pulp stimulation as presumably painful stimulus. The effect of trigeminal tractotomy on dental sensation is unknown. It is therefore impossible to propose a unified physiological schema for the mechanisms by which dental and facial stimuli are distinguished. The proposed research will employ psychophysical, physiological, and pharmacological techniques to study dental and facial sensory perception in monkeys with chronically implanted dental electrodes, before and after trigeminal tractotomy. The firing patterns of trigeminal neurons in response to identical stimuli will also be analyzed in acute experiments, after tractotomy. The study will help answer the crucial question about the effect of trigeminal tractotomy on dental sensation and will allow correlation of sensory changes and neuronal firing patterns. This research is essential before a unified theory of the mechanism of dental and facial sensation can be proposed. A thorough understanding of the mechanisms of dental and facial pain is essential before efficacious means can be devised for treating the many patients who suffer from intractable pain related to dental disease, cancer of the head and neck and idiopathic pain syndromes such as trigeminal neuralgia, post-herpetic neuralgia, and anesthesia dolorosa.

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10.0022, GUSTATORY CHEMOSENSITIVITY OF THE ORAL PALATE

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The word 'palatability' is associated with the perception of pleasant tastes, but the amount of information concerning the contribution of the palatal taste receptors to the gustatory sense is meager. Taste buds are present on the oral palates of humans and the human palate is as sensitive to chemical solutions as the tongue. In the rat which is frequently used as an animal model for the study of taste, there are as many taste buds on the palate as on the anterior part of the tongue. In these experiments the chemical sensitivity of the oral palate of the rat is examined by recording summated nerve response from the greater superficial petrosal branch of the facial nerve while chemical solutions are applied to the palatine surface. Concentration-response relationships are determined for sodium chloride, ammonium chloride, sucrose, hydrochloric acid and quinine hydrochloride. Three separate populations of taste buds are located on the palate which are designated the nasoincisor ducts, the Geschmacksstreifen or 'taste strip', and the posterior palatine field. Each population is individually stimulated with a region stimulator and the regional responses from the great petrosal nerve are determined from the summated response. The regional distribution of nerve fibers to the palate is reconstructed using silver staining techniques. Degeneration experiments indicate that there is considerable overlapping of nerve fibers from bilateral sources and from separate branches in the rostal-caudal axis. With high densities of taste receptors and overlapping innervation there seems to be present the requisite elements for lateral taste interactions which have been studied in this laboratory among fungiform receptors of the anterior tongue.

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10.0023, FACTORS AFFECTING DENTAL POSTOPERATIVE PAIN

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The present proposal outlines a series of studies designed to evaluate the perceived variability of post-operative oral-surgical pain.

Two lines of basic research in pain have recently converged; first, the discovery in the brain of endogenous opiate-like compounds (endorphins); and second, the analysis of a neural substrate that underlies an endogenous analgesia-producing system. Both human and animal studies indicate that the action of the analgesia-producing system is partially mediated by endorphins. We propose to investigate in detail the hypothesis that an endorphin-mediated analgesia system (EMAS) accounts for a significant part of the variability of perceived dental post-operative pain.

The experimental paradigm used in all the proposed experiments is based on manipulation and evaluatin of pain following extraction of impacted mandibular third molars. As in our previous work, pain will be assessed with a battery of subjective rating scales.

Our preliminary work has shown that the relatively pure narcotic-antagonist naloxone enhances post-operative pain in opiate-naive patients. These early studies also suggested that what is referred to loosely as the analgetic placebo may be mediated by an EMAS. We propose to extend these studies to investigate dose-response, time course and other characteristics of the human EMAS. Behavioral, pharmacological, and physiologic variables will be manipulated and/or measured in a controlled environment, in order to systematically evaluate the factors which contribute to the pain experience. We propose to study factors which activate the EMAS and evaluate its possible contribution to placebo and opiate analgesia.

This work will privide information that directly bears on behavioral and pharmacological management of post-operative pain.

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Research $97,554

10.0024, OPIATE ACTION ON CNS TERMINALS OF TOOTH PULP FIBERS

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This project seeks to determine if the central terminals of primary afferent fibers carrying nociceptive information to the CNS are a site of analgesic action of the opiates and opiate peptides. Attention is specifically directed at afferents from the tooth pulp since these fibers are known to conduct impulses primarily, if not exclusively, related to pain. The excitability testing technique will be used to determine the direct action of topically applied opiate on the polarization of central terminals of pulpal afferents. We will also assess the capacity of opiate to modulate the depolarization of these terminals caused by: 1) Topical application of transmitters believed to mediate primary afferent depolarization (PAD) and 2) By electrical stimulation of PAD pathways and of brain stem nuclei known to be involved in opiate analgesia. Induction or re-enhancement of PAD in these nociceptice afferent terminals by opiate would be expected to cause analgesia by decreasing transmitter release from the terminal. Such decrease will be measured directly by assay of putative primary afferent transmitters (glutamate, substance P, somatostatin) released during selective simulation of the dental pulp.

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10.0025, DENTAL PAIN - STUDIES ON TRIGEMINAL NUCLEUS CAUDALIS

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Tooth pulp afferents are known to project to nucleus caudalis, (in addition to other regions of the trigeminal nucleus), a region believed to play a major role in pain processing of oral-facial stimuli. However, many questions concerning the processing and relay of tooth pulp input with the nucleus still remain unanswered. It is the aim of this project to study the distribution of tooth pulp afferents to the nucleus caudalis, the responses of neurons in the nucleus to tooth pulp stimulation and the projection targets of these neurons. The interaction and convergence of tooth pulp input with activity arising from skin and other brain regions will also be investigated in order to determine what modulatory mechanisms exist. The experiments will involve standard electrophysiological recording techniques in anaesthetized cats. Glass-coated tungsten microelectrodes will be used to record from neurons in the superficial layers of the nucleus. Stimulating electrodes will be placed in tooth pulps, infraorbital nerve, thalamus, periaqueductal gray, nucleus raphe magnus and skin in order to determine the interaction of other regions and the the projection site of the neurons. The results of this study will help explain the neurophysiological basis of dental pain as well as other pains such as trigeminal neuralgia for which tooth pulp input may share a common path or at least serve as a useful model. These studies may also provide new insights into, and possible improvements of, the recent methods of transcutaneous nerve stimulation and brain stimulation produced analgesia being used to treat some pain conditions.

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Research $24,686

10.0026, ROLE OF SALIVA IN HUMAN TASTE PERCEPTION

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The proposed research has dual objectives. The first objective is to identify gustatory, olfactory and oral trigeminal stimuli which influence salivary flow in humans. Whole-mouth salivary flow and parotid gland secretion rates will be measured after exogenous stimulation. The second research objective is to evaluate the effects of salivary flow on human taste perception by measuring the gustatory recognition thresholds and taste preferences of patients receiving medications which alter salivary flow.

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10.0027, CHANGES IN BRAIN AMINES BY DENTAL LOCAL ANESTHETICS

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This study is designed to show a relationship between local anesthetic induced convulsions and changes in brain amines, i.e., serotonin, norepinephrine, and dopamine. Approximately 1120 male Sprague-Dawley rats will be used and only rat brain regions will be analyzed (when appropriate) for the three amines. Brain regions to be analyzed consist of the cerebral cortex, striatum, midbrain, hypothalamus, cerebellum, and pons-medulla oblongata. A total of fourteen experiments are planned and consist of: 1) Dose-response curves with lidocaine challenge and manipulation of brain serotonin; 2) Dose-response curves with lidocaine challenge and manipulation of brain norepinephrine and dopamine; 3) Time-course measurement of steady-state levels of the three amines in brain regions with lidocaine challenge; 4) Synthesis rate of serotonin in brain regions with tranylcypromine alone and with lidocaine; 5) Synthesis rate of serotonin in brain regions with probenecid alone and with lidocaine; 6) Time-course depletion of norepinephrine and dopamine in brain regions by alpha-methyl-p-tyrosine alone and with lidocaine; (7) Time-course depletion of norepinephrine in brain regions by FLA-63 alone and with lidocaine; 8) Repeat of the seven experiments with the drug procaine instead of lidocaine. The over-all objective is to characterize the mechanism of induction of local seizures at the level of a brain pathway in a particular region of rat brain.

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Research $33,071

10.0028, NOCTURNAL MASSETER MUSCLE ACTIVITY AND JAW DYSFUNCTION

G.T. Clark, University of California, Los Angeles Campus, School of Medicine, Division of Restorative Dental Sciences, *2025 Zonal Ave., Los Angeles, California* 90024 (R23 DE 05036-01A1)

The objective of this study is to investigate the specific relationship between nocturnal masseter muscle activity, and the signs and symptoms of abnormal jaw muscle function in normal subjects and subjects with myofascial pain.

The methods of this project include using a portable cummulative EMG device to establish the average level of masseter muscle activity over a two week period during normal sleep. A measure of the maximum bite force and a measure of the subject's fatigability and his kinesthetic sense will be performed. These measures will be performed on approximately 40 subjects with the absence of any subjective symptoms of jaw dysfunction and in 60 patients who complain of abnormal jaw muscle function but have no TMJ intracapsular dysfunction. An epidemiologic type index will be used to score and evaluate the symptoms of dysfunction along with the occlusal characteristics on all subjects. These subjects will be directed towards establishing levels of nocturnal muscle activity and measures of jaw muscle function in normal and symptomatic subjects. The symptomatic subjects will undergo 6 weeks of treatment either with exercises or an occlusal splint and a followup post-treatment evaluation will be performed on all subjects.

In summary, it will be of interest to relate the amount of nocturnal masseter muscle activity to the signs and symptoms of jaw dysfunction. These measures of jaw muscle function will serve as pretreatment records so that any change may be examined for and compared after routine treatment for myofascial pain. This information will hopefully answer the following two questions: 1) 'Is there a constant relationship between nocturnal muscle activity, abnormal jaw muscle function and the symptoms of myofascial pain dysfunction, and 2) what effect does occlusal splint therapy vs. exercise-heat therapy have on this relationship, if any.

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Research $32,002

10.0029, NEURAL CONTROL OF MANDIBULAR MOVEMENT

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This research is aimed at gaining an understanding of the neural mechanisms involved in the production of cyclic jaw movement and at gaining an understanding of the mechanisms used to produce the fractionation activity in bilateral pairs of jaw closing muscles which is necessary for the production of lateral jaw movements. Guinea pigs are trained to sit quietly and masticate small pieces of food while jaw movements are monitored using an optically coupled tracking system. Parameters of jaw movement are related to EMG patterns in the jaw closing muscles and to patterns of activity of neurons in several brain centers which might be part of an neural pattern generator for mastication. Lesions and microstimulation of these brain centers are also used to provide information about possible pattern generator activity. Lesions and microstimulation of the face area motor cortex are used to determine the function of this area, particularly in reference to lateral jaw movement. Degeneration stains are used following cortical lesion to determine the subcortical connections of this area cortex.

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Research $18,942

10.0030, ANATOMICAL STUDIES OF THE MAIN SENSORY AND SPINAL TRIGEMINAL NUCLEI

S. Gobel, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Neurocytology & Experimental Anatomy Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00020-14 NA)

This project is concerned with the synaptic connections of the sensory root of the trigeminal nerve and the morphology of the neurons which comprise the main sensory and spinal trigeminal nuclei. These studies employ electron microscopy, the Golgi method and the use of intraneuronal markers such as horseradish peroxidase. The objects of these studies are to delineate trigeminal pain-temperature pathways and to broaden our understanding of oral-facial sensation.

BIBLIOGRAPHIC REFERENCES: Gobel, S.: Neural circuitry in the substantia gelatinosa of Rolando: Anatomical Insights. In: Advances in Pain Research and Therapy, Vol. 3, edited by J.J. Bonica. Raven Press, 1979, in press. Gobel, S. and W.M. Falls: Anatomical observations of horseradish peroxidase filled terminal primary axonal arborizations in layer II of the substantia gelatinosa of Rolando. Brain Res., 1979, in press.

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10.0031, DESIGN AND COMPUTER INTERFACING OF NEUROPHYSIOLOGIC INSTRUMENTATION

F.J. Brown, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Neural Mechanisms Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00031-11 NA)

This work involves the development of suitable electronic and electro-mechanical instrumentation to be used in neurophysiological, physiological and behavioral research. It involves the adaptation and interfacing of these and other instruments to a laboratory or multipurpose computer installation.

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10.0032, ACTIVITY OF TRIGEMINAL AFFERENT FIBERS IN RESPONSE TO NOXIOUS AND INNOCUOUS STIMULI

R. Dubner, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Neural Mechanisms Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00040-10 NA)

Under barbiturate anesthesia, microelectrode recordings from the trigeminal ganglion of monkey are performed and electrical activity is recorded and stored on magnetic tape. Thermal and noxious heat stimuli are delivered with a precisely-controlled thermode which has a temperature range of 20 degrees C to 60 degrees C and can produce a temperature change of 10 degrees C at the thermode-skin junction within one second. Data are analyzed with the aid of an on-line real-time computer system. In related experiments, intracellular recordings are made from primary afferent neurons in trigeminal dorsal root ganglia, dorsal root fibers, or the spinal trigeminal tract, in response to innocuous and noxious thermal and mechanical stimuli. After functional characterization, horseradish peroxidase is iontophoresed into the cell or fiber. This intracellular label is then located in histological material and the central terminal projections of each axon determined.

BIBLIOGRAPHIC REFERENCES: Dubner, R., Sessle, B.J. and Storey, A.T.: The Neural Basis of Oral and Facial Function. Plenum Press, New York, 1978, 483 pp.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$58,733

10.0033, NEUROPHYSIOLOGY AND PSYCHOPHYSICAL SOFTWARE USED TO QUANTIFY AND CORRELLATE PAIN

S.A. Taylor, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Scientific Systems Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00056-08 OD)

The objective of this project at present has been the replacement of a single user software system to measure and analyze pain by a multi-user system which is capable of running two clinical pain laboratories as well as two data analysis centers simultaneously. The present software requirements have necessitated the acquisition of additional hardware (core memory, disk storage and another terminal) which will be installed shortly, as well as a redesign of some existing hardware in order to handle the multiple laboratories.

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10.0034, TRIGEMINOTHALAMIC NEURONS RESPONSIVE TO INNOCUOUS AND NOXIOUS STIMULI

D. Hoffman, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Neural Mechanisms Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00151-05 NA)

This project studied the responses of trigeminal nucleus caudalis neurons to noxious and innocuous mechanical and thermal stimuli in awake behaving rhesus monkeys. Monkeys were trained to detect the termination of innocuous heat stimuli and the onset of noxious heat stimuli. In a second task, the same monkeys detected the onset of a light stimulus while behaviorally nonrelevant thermal stimuli were presented. Nociceptive neurons exhibited thermal thresholds of 45 degrees C or lower and monotonic stimulus-response functions to noxious stimuli presented during both tasks. Responses to thermal stimuli presented during the light task were reduced in magnitude when compared to responses during the thermal task. A second class of neuron exhibited its maximum activity during the execution of task-related behaviors. This activity was independent of stimulus characteristics and could be separated from motor activity. Nociceptive neurons also exhibited task-related activity, but it was of lesser magnitude than the responses to noxious thermal stimuli. The task-related responses of both classes of neurons may be associated with attentional processes involved in organizing goal-directed behaviors.

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Compounds, edited by R.F. Beers and E.G. Bassett, Raven Press, New York, 1979, pp. 157-169. Hayes, R.L., Price, D.D. and Dubner, R.: Behavioral and physiological studies of sensory coding and modulation of trigeminal nociceptive input. In: Advances in Pain Research and Therapy, Vol. 3, edited by J.J. Bonica et al, Raven Press, New York, 1979, pp. 219-243.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$117,417

10.0035, ANATOMICAL STUDIES OF POSTNATAL MATURATION IN THE SPINAL TRIGEMINAL NUCLEUS

W.M. Falls, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Neurocytology & Experimental Anatomy Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00166-04 NA)

These studies examine the postnatal development of neurons in trigeminal pain pathways in the dorsal horn of the medulla (trigeminal nucleus caudalis) with Golgi and electron microscopic techniques. They compare in newborn kittens the maturity of the two major interneurons in the substantia gelatinosa (the stalked cell and the islet cell) with their adult counterparts. They follow the development sequences in the formation of the dendritic and axonal arbors of both stalked cells and the islet cells and examine how these interneurons eliminate excess dendrites as well as how they provide additional plasma membrane for their elongating dendrites and axons. These studies also determine which components of the synaptic circuitry in trigeminal pain pathways are present at birth and which develop postnatally.

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X. PAIN CONTROL & BEHAVIORAL STUDIES

10.0036, PHARMACOLOGICAL CHARACTERIZATION OF AXONAL ENDINGS IN TRIGEMINAL NUCLEUS CAUDALIS

M.T. Ruda, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Neurocytology & Experimental Anatomy Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00207-03 NA)

This study attempts to pharmacologically characterize axonal endings in the dorsal horn of the medulla (DHM). The methods employed include light and electron microscopic autoradiographic localization of labeled axonal endings in the DHM following application of tritiated (3H) neurotransmitters onto the DHM and immunohistochemical localization of specific populations of axonal endings. The neurotransmitters being investigated include serotonin, norepinephrine, enkephalin and substance P. The purpose of these studies is to locate and morphologically characterize pharmacologically distinct axonal endings in the DHM which might be involved in trigeminal pain pathways.

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10.0037, CYTOMORPHOLOGY OF FUNCTIONALLY CHARACTERIZED SPINAL CORD DORSAL HORN INTERNEURONS

G.J. Bennett, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Neural Mechanisms Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00247-02 NA)

Neurons in the spinal cord dorsal horn of monkeys and cats, especially neurons in lamina I and the substantia gelatinosa (SG), have been functionally characterized and intracellulary stained with horseradish peroxidase. The dendritic arbors and axonal extensions of these functionally identified neurons have been examined at the light microscope level. Wide dynamic range neurons, responsive to innocuous stimuli but activated maximally by noxious stimuli are found in layers I-V of the dorsal horn and have more extensive arbors than neurons in the same layers activated only by noxious stimuli (nociceptive-specific). The cytomorphological analysis of these functionally characterized neurons will soon be extended to the level of resolution of the electron microscope.

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10.0038, HORSERADISH PEROXIDASE STUDIES OF TRIGEMINAL PAIN PATHWAYS

S.J. Hockfield, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Neurocytology & Experimental Anatomy Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00248-02 NA)

This project examines the neural circuits involved in the appreciation of oral-facial sensations, particularly the circuits mediating pain and temperature sensations. Incoming sensory information may be modified by neuronal activity in many areas of the nervous system before being relayed to higher brain centers. Neuron marking techniques, in which a foreign protein (horseradish peroxidase) is picked up by axonal endings and carried back to their neuronal cell bodies, accurately demonstrate which neurons participate in a given neural circuit. Previous experiments in this study identified the neurons that relay incoming oral-facial sensations to higher brain centers. Experiments conducted during the past year have identified the neurons that can modify incoming sensory information and that may, in part, mediate analgesic and hyperalgesic states.

BIBLIOGRAPHIC REFERENCES: Hockfield, S. and Gobel, S.: Neurons in and near nucleus caudalis with long ascending projection axons demonstrated by retrograde labeling with horseradish peroxidase. Brain Research, 139: 333-339, 1978.

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10.0039, EXPERIMENTAL INVESTIGATION OF PAIN

W.W. Kaelber, University of Iowa, School of Medicine, Dept. of Anatomy, *Jessup Hall, Iowa City, Iowa* 52240 (R01 GM 23336-04)

This continuing project is aimed at a greater understanding of the role that various portions of the brain, especially the mesencephalon and diencephalon, play in the conscious awareness of pain. The research is concerned primarily with an investigation of the neurons and fiber tracts involved in the production of pain that are not basically related to the classical neospinothalamic tract. These are, and have been, studied by (1) behavioral-shaping electrical stimulation of intracranial subthalamic, pulvinar (intralaminar system to be covered), tooth pulp (trigeminal) and radial nerve, (2) neuropharmacological drugs, (3) lesions of the most pertinent brain areas to determine if there is a block of escape (nociceptive) versus non-nociceptive behavior, as well as to evaluate changes in these behaviors that may occur long after an 'effective' lesion, and (4) tracing of axonal fibers relevant to nociception.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of General
Medical Sciences $70,066

10.0040, BRAIN STEM MECHANISMS OF TRIGEMINAL NOCICEPTION

S.G. Nord, State University of New York, Upstate Medical Center, School of Medicine, Dept. of Neurology, *766 Irving Ave., Syracuse, New York* 13210 (R01 NS 10814-06)

The objective of our research is to discover how the various components of the sensory trigeminal complex operate in the mediation of oro-facial sensation, particularly pain. To this end, we have been carrying out two concurrent programs of research. The first utilizes electrophysiological procedures to study the responses of pontine and bulbar neurons to noxious and innocuous peripheral stimuli. Acute experiments are performed upon lightly anesthetized, immobilized cats and monkeys. The second program makes use of monkeys with surgically implanted dental stimulating electrodes. The awake, unanesthetized animals are studied in an operant (escape) paradigm while behavioral responses to graded electrical tooth stimulation are recorded. After consistent response patterns are established, the animals are studied in acute, electrophysiological experiments, as above. Ultimately, behavioral, physiological and anatomical data are analyzed and inter-related.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,

best copy available

National Inst. of Health,
National Inst. of Neurological
& Communicative Dis. &
Stroke $68,337

10.0041, PERIPHERAL MECHANISMS IN TASTE RECEPTION

J.G. Brand, Monell Chemical Senses Center, *3500 Market St., Philadelphia, Pennsylvania* 19104 (R01 NS 15565-01)

The sense of taste is active in food recognition, in motivating ingestion and triggering certain reflexive digestive processes. In spite of recent advances, however, our knowledge of the peripheral biochemical mechanisms in taste is inadequate. While a receptor hypothesis is attractive, receptor macromolecules unique to taste receptor cells have not been demonstrated. Also, the biochemical mechanisms operative during transduction of the chemical message through the taste cells to the innervating nerve are not understood. This proposal plans to use fluorescent probe techniques in an attempt to gain information about these events. We will use a system which permits the observation of either intrinsic or extrinsic fluorescence from taste buds in situ. Recent work has suggested that ions imparting a salty taste change the levels of reduced pyridine nucleotide in the circumvallate papillae from bovine tongue. We will explore further the nature and specificity of this change. Fluorescence from extrinsic sources, either as dyes or as stimuli, can also be used in this intact system to observe the interaction of stimulus with receptor or, in the case of nonstimulating and passive dyes, to monitor the transductive event. Experiments using bitter stimuli will attempt to explore further the binding specificity for this modality. Collaborative efforts are planned with morphologists and neurophysiologists. Our ultimate aim is to find fluorescent agents which can passively label taste cells in situ and report their activity toward stimulating chemicals.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Neurological
& Communicative Dis. &
Stroke $67,519

10.0042, NEURAL MECHANISMS OF ORO-FACIAL PAIN

M.A. Biedenbach, University of Texas, Health Science Center at San Antonio, South Texas Medical School, Dept. of Physiology, *7703 Floyd Curl Dr., San Antonio, Texas* 78284 (BNS78-06953)

X. PAIN CONTROL & BEHAVIORAL STUDIES

The aim of this study is to identify neural mechanisms that generate pain. This study will focus on the trigeminal system which receives somatosensory information from the face and oral cavity. Both painful and nonpainful stimuli will be applied to orofacial regions to establish the central representation of these stimuli in terms of single neuron potentials.

The total neuron population, which can be activated through the lingual branch of the trigeminal nerve and/or a canine tooth pulp will be investigated in two main areas of the brainstem: trigeminal nucleus and adjacent reticular formation. While searching for unit potentials, electrical stimuli will be applied to the lingual nerve and a canine tooth pulp so that all neurons can be identified that receive input via those two pathways. For each driven neuron, the exact location in the brainstem and responses to a standard set of electrical and mechanical stimuli will be recorded. Both nonnoxious (touch, pressure) and noxious (pinch, tooth pulp) stimuli are employed so that neural responses representing nonnoxious stimuli can be distinguished from those specifically representing noxious stimuli.

The data should contribute towards understanding the neural basis of pain and of procedures that relieve pain.

SUPPORTED BY
U.S. National Science
Foundation, Directorate for
Biological Behavioral & Social
Sciences, Div. of Behavioral &
Neural Sciences $0

10.0043, ORAL SENSORY RECEPTORS - MECHANISMS OF TASTE AND APPLICATIONS

R.H. Cagan, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *38th & Woodland Aves., Philadelphia, Pennsylvania* 19104 (642-001-P)

The sense of taste has important implications for human nutrition. Little has been know of the biochemical basis of taste, although an area such as sweet taste is especially important in clinical conditions of obesitiy and diabetes.

Our biochemical studies of taste show that initial recognition of taste compounds occurs at the level of the receptor cell membranes. Highly purified plasma membranes have been prepared from taste receptor tissue and shown to possess binding activity for taste stimuli.

Monellin is a sweet-tasting protein discovered in our laboratory and characterized during the past few years. Partial methylated protein. By incorporating a tritium (radioactive) label during the methylation, radioactively labeled protein has been prepared, enabling its binding to be measured to taste receptors.

The binding methodology that we developed for taste studies has been applied to the olfactory system, enabling determination of binding specificity of radioactively-labeled odorants to olfactory receptor preparations.

These studies provide a fundamental basis for the functioning of the taste and smell sensory systems, and could provide information useful in therapeutic management of clinical disorders of taste and smell.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

10.0044, THE NEUROPHYSIOLOGY OF ORAL STRUCTURES

D.J. Anderson, University of Bristol, Dental School, *Bristol, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$58,426

10.0045, INVESTIGATION INTO THE EFFECTS OF SYMPATHETIC EFFERENT ACTIVITY ON DENTAL MECHANORECEPTOR AFFERENT DISCHARGE

R.W. Linden, University of London, Guys Hospital Medical School, Dept. of Physiology, *London Bridge, London SE1 9RT, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council	$38,346

10.0046, PROPERTIES AND ROLE OF THE SENSORY ENDINGS IN THE TOOTH

C. Mei, Universite dAix Marseille, Faculte de Chirurgie Dentaire, Dept. of Biology & Fundamental Materials, *Charles Livon Blvd., Jardin Emile Duclaux, 13007 Marseille, France*

The aim of these investigations is to study the properties and the roles of the sensory endings located in the tooth. The microelectrode technique is applied to the gasserian ganglion in order to record the unitary discharges originating from the tooth. We have formerly investigated the properties of the periodontal receptors. Now, we are chiefly interested in the problem of the sensibility of the pulp and of the dentin. On the other hand, our laboratory has developed a new type of investigation concerning the role of the periodontal receptors, particularly in the osteomorphogenesis: regulation of the local circulation, control of the growth hormone release.

These studies are performed on anaesthetized animals: rats, cats and monkeys.

SUPPORTED BY

Universite dAix Marseille	funds n.a.

10.0047, AN IMPROVED SILVER IMPREGNATION TECHNIQUE FOR THE HISTOLOGICAL DEMONSTRATION OF NERVES

J.E. Linder, University of London, London Hospital Medical College, Dept. of Oral Pathology, *Turner St., London E1 2AD, England, United Kingdom*

Factors are being examined which may determine the specificity and quality of the silver impregnation of nerves in the central and peripheral nervous systems. An improved method showing consistent results has been applied to nerves in a variety of tissues; mammalian and lower vertebrate, adult and embryonic, decalcified and nondecalcified. Development of the method is continuing.

SUPPORTED BY

University of London	funds n.a.

10.0048, YOUNG CHILD'S RESPONSE TO DENTAL STRESS

L.L. Venham, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Pediatric Dentistry, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 04409-03)

The purpose of this project is to study the response of preschool children to dental stress. Children, 2 to 5 years old, with no previous dental experience will be studied longitudinally for three years during periodic dental visits. Three factors will be examined: 1) The effect of age on the child's response to the initial dental experience and to continued periodic dental care. 2) The effect of non-stressful exam visits on the young child's response to eventual stressful treatment procedures, and 3) The effect of stressful treatment experiences on children's response to subsequent dental care. The child's response will be assessed, using a combination of human figure drawing, clinical ratings of cooperative behavior. A multivariate analysis of variance for repeated measures will be used to test for significant effects.

Physiological, self-report and clinical measures. The physiological measures include heart rate, skin conductance, E.M.G. and skin temperature. The self-report measures are the picture test and the human figure drawing. The clinical measures include ratings of anxiety and cooperative behavior.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $78,422

10.0049, MASSETERIC EXTEROCEPTIVE REFLEX AND SENSORY RESPONSES IN MPD PATIENTS

P.A. McGrath, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Neural Mechanisms Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00246-02 NA)

The objectives of this project are: to establish sensory and pain thresholds to electrical tooth pulp stimulation in myofascial pain dysfunction (MPD) patients and to relate sub-sensory, sensory and pain producing stimuli of the tooth pulp to the masseteric inhibitory period in MPD patients, by means of electromyographic (EMG) recordings. In both these cases comparison between MPD patients to normal subjects will enable a better understanding of the MPD syndrome pain and dysfunction mechanisms, and the gain of insight into possible protective mechanisms of the inhibitory period.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $39,056

10.0050, ASSESSMENT OF EXPERIMENTAL AND CLINICAL PAIN

R.H. Gracely, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Neural Mechanisms Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00133-05 NA)

The objectives of this project are 1) to assess psychophysical methods of experimental pain measurement, i.e., magnitude estimation, category scaling, and cross-modality matching. Pain will be experimentally induced by electrocutaneous, electric tooth pulp, and mechanical heat stimulation; 2) to assess clinical pain measures, such as pain questionnaires and sensory matching methods, in a dental setting; 3) to determine the validity of experimental pain model by comparison of experimental and clinical pain responses; and 4) to evaluate known pharmacological and non-pharmacological pain-control agents.

BIBLIOGRAPHIC REFERENCES: Gracely, R.H., Dubner, R. and McGrath, P.A.: Narcotic Analgesia: Fentanyl Reduces the Intensity but not the Unpleasantness of Painful Tooth Pulp Stimulation. Science, 203:1201-1263, 1979.

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U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $109,689

10.0051, SENSATIONS PRODUCED BY TOOTH PULP STIMULATION

P.A. McGrath, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Neural Mechanisms Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00245-02 NA)

The objective of this project is to determine the nature of sensations produced by tooth pulp stimulation. Non-pain, as well as pain sensations are evoked when low intensity electric current is applied to human teeth. In order to assess the role of non-pain sensations in the pulp, a traditionally exclusive pain system, these sensations were studied both psychologically and physiologically: 1) the minimum levels of current necessary to produce non-pain and pain sensations were determined for different frequencies of stimulating current; 2) the intensities of sensations from detection threshold to pain threshold were scaled by magnitude production and by verbal descriptors; 3) electromyographic (EMG) activity of the masseter inhibitory period was recorded during tooth pulp stimulation at both non-pain and pain currents; 4) the effect of a narcotic on sensations produced by tooth pulp stimulation and on the masseter inhibitory period was evaluated; and 5) the effects of a conditioning electrical stimulus, applied to the tooth, on sensation and on masseteric inhibitory period were determined.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $31,952

10.0052, NARCOTIC AND BRAIN STIMULATION ANALGESIA ON HUMAN CHRONIC AND EXPERIMENTAL PAIN

R.H. Gracely, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Anesthesiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00276-01 NA)

The purposes of the study are (1) Assess the effectiveness of chronic electrical stimulation of midbrain sites for the relief of chronic pain in humans; (2) Evaluate the efficacy and mechanisms of traditional narcotic analgesia and compare these to chronic electrical stimulation of midbrain sites; (3) Validate experimental models of pain and their potential diagnostic use in chronic pain patients; and (4) Determine and compare the impact of both traditional narcotic and chronic electrical stimulation therapies on the functional, intellectual and emotional well being of these patients. Participants in this study will be (1) chronic pain patients receiving surgically implanted stimulating electrodes for pain control; (2) chronic pain patients maintained on traditional narcotic analgesics who will not receive implanted stimulating electrodes; and (3) healthy normal volunteers. The effects of chronic brain stimulation in surgical patients will be compared to the effects of narcotics previously administered to patients and to effects of narcotic regimes in nonsurgical chronic pain patients. In addition, the effects of narcotics on perceptual and neural mechanisms of experimentally induced pain and on normal psychological functioning will be compared between chronic patients and normal volunteers free of chronic pain.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$63,915

10.0053, ACUPUNCTURE AND PERCEPTION OF DENTAL PAIN IN MAN

C.R. Chapman, University of Washington, School of Medicine, Dept. of Anesthesiology/Psychiatry & Behav Scis & Psychology, *A-300 Health Sciences Ctr., SC-64, Seattle, Washington* 98195 (R01 DE 04004-05)

The objectives of this proposal are: 1. to extend our observations of acupunctural and transcutaneous electrically-induced dental analgesia; 2. to fully develop brain evoked potential measures of pain and analgesia for laboratory work; 3. to interrelate these measures with psychophysical Sensory Decision Theory measures; and 4. to further investigate the possible role of endorphins in stimulation-induced analgesia. During the past year we have examined the effects of electrical acupuncture stimulation on brain evoked response to experimental dental pain, and have attempted to determine whether this effect can be reversed by the injection of naloxone, a narcotic antagonist. Our findings support the hypothesis that acupuncture is in part mediated by the release of endorphins. We have also explored the relationship between Sensory Decision Theory and evoked potential methodologies, and our results suggest that these two research methods are tapping a singular perceptual process associated with pain and that the activity of the brain during the perception of laboratory-induced dental pain can be accurately modeled by the theoretical constructs of Sensory Decision Theory. We have also examined the effects of fentanyl, a narcotic analgesic, on the cerebral evoked potential and measured the reversal of this analgesia with naloxone. This provides a better understanding of the relationship between changes in cerebral evoked potential and narcotic analgesia. Our work is contributing to a better understanding of the relationship between changes in brain activity and changes in subjective pain, to growing information on acupuncture analgesia, and to an understanding of the relationship between psychophysics and brain evoked potential work. During the coming year we will continue our work on acupuncture analgesia and place a strong emphasis on further clarifying the relationship between Sensory Decision Theory and evoked potential measures so that this combined methodolgy can be used to study acupuncture analgesia.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$69,644

10.0054, EVALUATION OF ACUPUNCTURE THERAPEUTICS

L.Y. Chen, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Rehabilitation Medicine Service, *800 Poly Pl., Brooklyn, New York* 11209 (527-001-F)

Acupuncture was used as a therapeutic measure for teatment of different conditions. Specific acupuncture points were used with size 30 stainless steel acupuncture needles with or without electrical stimulation, according to the different conditions.

From June 1974 to February 1979 a total of 82 were evaluated and treated. Tabulated results are attached.

Out of the 82 patients treated with acupuncture, 72% showed good results; 16% fair result and 12% poor result.

Good results were obtained through acupuncture treatment of low back pain, tennis elbow, trigeminal neuralgi & post herpezoster neralgia. Although there were cases of recurrence of low back pain, these patients came back after intervals of 2-3 months to get another series of acupuncture. They indicated their preference for acupuncture treatment than to any other modalities or medication. One of the patients suffered from CVA with right hemiparesis and hemisensory deficit. He claimed that he regained sensation in his right hand after acupuncture. This mechanism is not known and cannot be reproduced; (i.e., the same result in another patient with similar condition). The result in treating neurological conditions such as Multiple Sclerosis, stroke with hemiplegia, deafness and organic brain syndrome is poor. No benefit is noted in treatment of phantom pain.

No incidents involving morbidity, mortality and other side effects were noted during this research period.

CONCLUSION: Acupuncture has therapeutic value for relief of chronic pain. Its mechanism is not clear. Under strict aseptic technique the side effects or complication are negligible.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

PATHOLOGY - PHARMACOLOGIC AGENTS

10.0055, RESEARCH AND DEVELOPMENT IN PREVENTIVE DENTISTRY

J.R. Lawter, Abcor Inc., *850 Main St., Wilmington, Massachusetts* 01887 (TO BE DETERMINED)

The objective of this study is to microencapsulate lidocaine in a bioadsorbable polymer that will result in slow release and consequent anesthesia for up to several days.

The encapsulation will be accomplished by an air suspension coating process. The anesthetic encapsulated polymer will be tested in rats by the method of camougis and takmin (1971). Drug release rates will be determined by suspending a known mass of microcapsules in a known volume of an aqueous solution and periodically measuring the concentration of the drug released by spectrophotometry.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command	$47,498

10.0056, BIOLOGICAL EFFECTS OF NITROUS OXIDE USED IN DENTISTRY

A.C. Verrusio, American Dental Assn., Health Foundation, Division of Developmental Biology, *211 E. Chicago Ave., Chicago, Illinois* 60611 (R01 OH 00742-02)

A recent survey of dentists suggested that occupational exposure to anesthetic gases might be a health hazard to the dentist, the dental staff, and their families. Since nitrous oxide is the oldest and the most widely used anesthetic agent in the current dental practice, there is a need for continual review of the long-range biological effects of low-level nitrous oxide exposures. The proposed research project will initiate the following multidisciplinary investigations regarding the biological effects of low-level exposures of nitrous oxide in a systematic fashion: a) genetic effects in two inbred strain of mice and Sprague-Dawley rats, b) development effects on mouse and rat embryos, and c) morphological and biochemical effects on the liver, lung, kidney, testes and drug-metabolizing enzymes of mice and rats.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health	$55,039

10.0057, THE CENTRAL MECHANISMS OF DENTAL PAIN AND ANALGESIA

V.A. Lewis, University of Texas, Health Science Center at Houston, Dental Branch, Dept. of Pharmacol, *6515 Freeman, Houston, Texas* 77025 (R23 DE 04646-03)

This proposal describes a neurophysiological investigation of the mechanisms of orofacial pain and analgesia for the purpose of generating information upon which a unifying hypothesis of sensory transmission within the trigeminal nuclei can be built. Current evidence suggests that significant modification of sensory messages in the trigeminal nuclei by both the central nervous system and intranuclear mechanisms can occur. By employing descriptions of the microstructure of the trigeminal nuclei as a guide for placement of electrodes, recordings of electrical activity in the trigeminal nuclei under varying physiological and drug induced states will be evaluated to determine the nature of the data transformation (i.e., the transfer function) at these loci. Because pain is a conscious sensation a chronically implanted rat preparation will be employed. A neurometeric anaysis utilizing EEG, evoked potential and multiple unit recordings will be undertaken. Treatments influencing pain transmission to be evaluated are: locally microinjected analgesics, focal brain stimulation and electrolytic lesions. Changes in bioelectric activity after tooth pulp stimulation will be correlated with changes in behavior after tooth pulp stimulation previously characterized. Upon completion of these studies a clearer understanding of the mechanisms of orofacial pain and analgesia can be developed which will aid the clinician in treating pain more rationally.

BIBLIOGRAPHIC REFERENCES: Vahn A. Lewis and G. F. Gebhart, Morphine-induced and stimulation produced analgesias at coincident of periaqueductal central gray loci: Evaluations of analgesic congruance, tolerance and cross tolerance. Experimental Neurology 57, 934-955 (1977).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$13,952

10.0058, NEUROPHARMACOLOGICAL ANALYSIS OF SUPRASPINAL AND NARCOTIC MODULATION OF PAIN

R.L. Hayes, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Neural Mechanisms Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00165-04 NA)

The major concern of this project was twofold: 1) to develop a primate, behavioral model of pain in which the animal's response to noxious stimuli is primarily, if not totally, dependent upon the sensory (intensity) dimension of pain while independent of the affective dimension of pain; 2) to test the hypothesis that narcotic analgesics (viz. morphine) can suppress the sensory (intensity) dimension of noxious heat stimuli. A corollary of this hypothesis that altering the affective state by minor tranquilizers, like diazepam, is not sufficient to suppress the sensory (intensity) dimension of pain was also tested. Techniques employed in this study were application of thermal heat via contact thermode, using latencies as a behavioral index of perceptual sensitivity, i.m. injections of drugs, and real-time computer control of the experimental sessions. The objectives of this study were to develop a more comprehensive behavioral model of pain in animals (primates) and to broaden our understanding of the analgesic action of narcotics.

BIBLIOGRAPHIC REFERENCES: Hayes, R.L., Bennett, G.J., Newlon, P.G. and Mayer, D.J.: Behavioral and physiological studies of non-narcotic analgesia in the rat elicited by certain environmental stimuli. Brain Research, 155:69-90, 1978. Yayes, R.L., Price, D.D., Ruda, M.A. and Dubner, R.: Suppression of nociceptive responses in the primate by electrical stimulation of the brain on morphine administration: behavioral and electrophysiological comparsons. Brain Research, 167:417-421, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$15,079

10.0059, EVALUATION OF SAFETY AND EFFICACY OF TYLENOL, ACETAMINOPHEN WITH ELIXIR, COMPARED TO EMPIRINE COMPOUND WITH CODEINE

G.C. Hornbuckle, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *921 N.E. 13th St., Oklahoma City, Oklahoma* 73104 (635-001-I)

The objective of this study is to determine the safety and efficacy of Tylenol with codeine elixir as compared to Empirin Compound with codeine phosphate 03 and to placebo in the treatment of moderate to severe pain secondary to oral surgical procedures.

The investigators will study 21 patients who have pain secondary to oral surgical or other dental procedures with which pain of moderate to severe intensity is anticipated. Patients will remain at the treatment facility during the observation period. The patient will be interviewed by the investigator or nurse-observer and an inquiry will be made as to the amount of pain present. If the patient indicates moderate or severe pain, he or she will be entered onto the study and a single dose of medication will be administered. Patients will report pain level, pain relief, and any adverse effects for four hours after medication is given. If after two hours the patient has experienced no relief from pain he will be medicated with other analgesics and his participation in the trial will be terminated. If a limiting adverse reaction occurs, the patient's participation in the trial will be terminated.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

PATHOLOGY - ORAL-FACIAL PAIN SYNDROMES

10.0060, TRIGEMINAL NEURALGIA

E. Ratner, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Facial Pain Clinic, *800 Poly Pl., Brooklyn, New York* 11209 (527-001-P)

Dramatic progress continues in the treatment of the facial neuralgias. An increasing body of data is being accumulated which implicates the causative pathology of the facial neuralgias in pain syndromes throughout the body, as well as in visual, auditory and vestibular dysfunction. New pain referral tracts have been defined which are discreet, reproducible and serve as the primary basis for pathology localization. As a result of data dissemination from this program, massive replication of our results has occurred. Despite massive replication, it must be emphasized that a transition from empirical to rational therapeutics must be achieved. The major requirement of such transition is the development of techniques for rapid bacterial culture and antibiotic sensitivity determinations. Facilities adequate for these studies do not presently exist within the Veterans Administration and cannot be established with the funding presently available. A request will be forthcoming for application of portion of current research funds as a Purchase Order for services to the Leahy Clinic. We have collaborated with the Leahy Clinic for the past year in the development of equipment for rapid bacterial culture and sensitivity determinations. As a result of research derived from this program, the Veterans Administration now leads the world in two major areas of pain therapy. With adequate support and expansion of research, the Veterans Administration can emerge as the major organization in the world in the understanding of the neurophysiology of pain. Without support, the work which began here will be completed elsewhere.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

DIAGNOSIS & TREATMENT - DENTAL FEAR & ANXIETY SYNDROMES

10.0061, ACUTE PAIN IN RESEARCH AND CLINICAL SETTINGS

S.F. Dworkin, University of Washington, School of Dentistry, Dept. of Psychiatry & Behavioral Sciences, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (P01 DE 05130-010006)

The primary objective of this research proposal is to measure physiologic and behavioral responses to pain when the pain is experienced in an experimental laboratory versus a 'real' clinical setting. A series of largely parallel experiments is proposed to be conducted in the context of (1) a human research pain laboratory where experimental pain can be elicited from teeth, and (2) a clinical dental treatment context, where equivalent 'real' pain is generated during actual dental treatment.

Within both the laboratory and clinical contexts, chemotherapeutic and psychological interventions will be systematically introduced. These interventions include controlled use of chemosedation techniques common for pain control in dentistry and manipulation of psychological variables such as situational context, hypnosis, information, and subject control over painful events.

Changes in physiologic functioning (e.g. heart rate, blood pressure, respiration, blood chemistry, EEG) and observable behavior (e.g. cognitive functioning, report of pain and anxiety) will be measured and evaluated by several data-analytic methods, including signal detection theory.

Experimental pain will be induced by electrical stimulation of the teeth in both the laboratory and clinical settings, and clinical dental pain will be induced by dental therapies in the clinical dental context.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$111,913

10.0062, THE ASSESSMENT AND TREATMENT OF FEAR OF DENTISTRY

R.A. Kleinknecht, Western Washington University, School of Arts & Sciences, Dept. of Psychology, *516 High St., Bellingham, Washington* 98225 (R01 DE 04014-04)

The proposed and in-progress research involves investigation of multichannel assessment of dental fear in adults which are used as dependent variables in factorial comparisons of the relative efficacy of three fear reduction treatment packages. The three treatment packages include participant modeling, symbolic modeling and graduated exposure. These treatments will be compared with two control conditions: (1) an attention placebo treatment called 'stress-tolerance training' and (2) Positive Dental Experience in which the fearful patient is referred for an actual appointment with a practicing dentist. Following the outocme of this study, we propose to test a short-term treatment package composed of the most effective portions of the treatments previously investigated in order to develop an efficient, practical treatment program usable by practicing dentists.

Concurrent with the treatment studies we propose to continue investigation of assessment procedures to identify a set of behavioral indices which best differentiates fearful from non-fearful dental patients.

BIBLIOGRAPHIC REFERENCES: Early, C. E. and Kleinknecht, R. A. The Palmar Sweat Index as a Function of Repression-Sensitization and Fear of Dentistry. Journal of Consulting and Clinical Psychology, 1978, 46, 184-185.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research
$0

10.0063, SYSTEMATIC DESENSITIZATION OF DENTAL FEARS

E. Jackson, Temple University, School of Dentistry, *3223 N. Broad St., Philadelphia, Pennsylvania* 19122 (R01 DE 04143-03)

Recognizing the enormous burden placed upon health care delivery services by fear of the dentist, the proposed research aims to identify a practical method of eliminating dental fears in the dental practice setting. We have shown in a laboratory situation that both the psychological procedure of systematic desensitization and a more cognitive approach called stress management are effective for reducing the fears of dental phobics.

The proposed research will involve the development of systematic desensitization and stress management procedures that can be utilized in dental practice, and the thorough evaluation of those procedures for reducing the fear of average dental patients, and the impact of the programs in aiding the dentist in providing care efficiently.

Manipulations: In a controlled experiment with fearful dental patients in average dental practices, a systematic desensitization procedure and a stress management procedure will be evaluated against two control groups.

Measure: Assessment of patients' fears and dental health will be performed prior to and subsequent to the psychological manipulations.

Changes in the dentist's perception of the patients' cooperativeness and the percentage of the dentist's time spent actually providing care will be assessed.

Upon follow-up examination (one year) the long-term effectiveness of the treatment will be assessed by a further assessment of patients' psychological orientation and dental health.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research
$0

10.0064, BEHAVIORAL APPROACHES TO PAIN RESPONSES IN PEDODONTICS

B.G. Melamed, Case Western Reserve University, Graduate School, Dept. of Psychology, *2040 Adelbert Rd., Cleveland, Ohio* 44106 (R01 DE 04243-03)

This study provided significant support for the potency of videotaped peer modeling in the modification of fear-related behaviors in children receiving dental treatment. The fact that there was evidence for greater effectiveness of the peer modeling conditions over the demonstration videotapes suggests that this effect involves more than the mere transmitting of information about what will occur. Children who had seen the peer models recalled more information than those viewing the demonstration tape. Since the effect is observed largely on the behavioral measures, it seems likely that the presence of the peer model allows for the child's observation of how to behave during the treatment.

The amount of information presented seems to have had a greater effect on the child's subjective report of fear. Children who viewed the videotapes that contained all the specifics about what would take place during the restoration were less anxious going into the treatment session than those who has been exposed only to the shortened version depicting the anesthetic injection and an oral examination. In fact, one is tempted to speculate that the short version may have sensitized the children to the impending treatment since there was a significant increase over their apprehension at the first visit to the clinic. Children viewing the longer, more informative tape were even less anxious prior to the treatment than they had been at the first visit.

These results suggest that specific information about the procedures to be undertaken, presented within a modeling context, will most likely decrease the child's subjective anxiety and produce greater cooperation during treatment even when dentists' behavior strategy is neutral.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
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National Inst. of Dental
Research
$0

10.0065, CONTROL OF STRESS DURING DENTAL PROCEDURES

N.L. Corah, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Behavioral Science, *3435 Main St., Buffalo, New York* 14214 (R01 DE 04494-03A1)

Stress during dental procedures is a problem for both the patient and the dentist. Many patients avoid the dental situation until they are forced to go because of their perception of the situation as stressful. This results in poor oral health. From the dentist's standpoint the difficult patient results in loss of time and unnecessary difficulty in executing necessary procedures.

The proposed research is designed to lead to the development of practical techniques for reducing patient stress in dentistry and similar health related treatment procedures. At the same time the research will increase our understanding of the mechanisms involved in stress reduction in situations which include potentially aversive stimulation.

Two approaches designed to reduce patient stress will be evaluated: 1) the use of relaxation instructions, and 2) the use of distraction. Two components of relaxation instructions will be evaluated: tempo of voice and instructional content. Three approaches to distraction: audio, audio-visual and active involvement in a video game will be evaluated. Finally, patient self-selection of procedure will be studied. In addition, patient variables will be investigated to see if different techniques are more successful with different types of patients. Physiological and behavioral indices will be used.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $43,665

10.0066, EFFECTS OF PHYSIOLOGICAL FEEDBACK ON DENTAL FEAR

R. Hirschman, Kent State University, School of Arts & Sciences, Dept. of Psychology, *Hilltop Dr., Kent, Ohio* 44240 (R01 DE 04769-02)

Ample evidence exists implicating treatment-related dental fear to difficulties in providing appropriate dental care. Unfortunately, the variety of presently available approaches to attenuate dental fear have not been sufficiently practical for in-office dental use. As such, the aim of the proposed research is to examine an alternate approach with potential practical utility. More specifically, veridical and nonveridical amplified signals of visceral activity will be used in the proposed experiments as reinforcements for visceral control, i.e., biofeedback, and for the attenuation of dental fear. This approach should help to clarify further the importance of cognitive mediation and utilization of visceral cues for emotional attribution and concomitant emotional experience. Furthermore, if these variables are critical for the self definition of emotional state, then if should be relatively easy to incorporate them into an applied procedure within time-frame restrictions required by the typical dental practitioner.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $44,585

10.0067, DENTIST VARIABLES AND FEAR IN CHILDREN

P. Weinstein, University of Washington, School of Dentistry, Dept. of Community Dentistry, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (R01 DE 04770-01A1)

This research is designed to identify functional and dysfunctional communication patterns between dental practitioners and children, and to determine the effects of dental practitioner variables of confidence and tolerance for various child behaviors on the fear related behavior of children.

These objectives will be accomplished by videotaping a series of three visits for 60 children, 30 with and 30 without a history of disruptive behavior, administering appropriate measures, and analyzing the data for 10 phases of treatment using Markov analyses and other procedures.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $53,778

10.0068, PAIN TOLERANCE IN THE TREATMENT OF DENTAL FEAR

R.K. Klepac, North Dakota State University, School of Science & Mathematics, Dept. of Psychology, *Fargo, North Dakota* 58102 (R01 DE 04976-02)

Pain Tolerance Training (PTT) and the procedurally-similar 'stress inoculation', demonstrably useful in increasing tolerance for certain fears and laboratory-induced pain, has been applied to dental phobias only at the case study level. The primary purpose of this research is to refine the procedure, then test its effectiveness in treating intense fear and avoidance of dental work. Three common stressors which have been used alternatively in PTT will be assessed for their relative effectiveness in training tolerance for dentally relevant, laboratory-induced pain. Then, in a factorial study, the three main components of PTT (relaxation, cognitive coping, stressed practice) will be evaluated for their effects on laboratory-induced pain, and the most parsimonious combination of components defined. This combination will then be tested against the full PTT package, the most promising alternative behavioral strategy, and appropriate control procedures in treating actual dental phobics. In the course of these studies, differences between fearful and non-fearful dental patients in pain sensitivity will be explored as well.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$62,478

10.0069, SYSTEMATIC DESENSITIZATION OF DENTAL FEARS

E. Jackson, Temple University, School of Dentistry, Dept. of Community Dentistry, *3223 N. Broad St., Philadelphia, Pennsylvania* 19122 (R01 DE 05546-01)

Recognizing the enormous burden placed upon health care delivery services by fear of the dentist, the proposed research aims to identify a practical method of eliminating dental fears in the dental practice setting. We have shown in a laboratory situation that both the psychological procedure of systematic desensitization and a more cognitive approach called stress management are effective for reducing the fears of dental phobics.

The proposed research will involve the development of systematic desensitization and stress management procedures that can be utilized in dental practice, and the thorough evaluation of those procedures for reducing the fear of average dental patients, and the impact of the programs in aiding the dentist in providing care efficiently.

Manipulations: In a controlled experiment with fearful dental patients in average dental practices, a systematic desensitization procedure and a stress management procedure will be evaluated against two control groups.

Measure: Assessment of patients' fears and dental health will be performed prior to and subsequent to the psychological manipulations.

Changes in the dentist's perception of the patients' cooperativeness and the percentage of the dentist's time spent actually providing care will be assessed.

Upon follow-up examination (one year) the long-term effectiveness of the treatment will be assessed by a further assessment of patients' psychological orientation and dental health.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

10.0070, COMPARING THE EFFICACIES OF CONSCIOUS SEDATION DRUGS

S.A. Cooper, College of Medicine & Dentistry of New Jersey, New Jersey Dental School, School of Dentistry, Dept. of Oral Surgery & Anesthesiology, *100 Bergen St., Newark, New Jersey* 07103 (R23 DE 05420-01)

Intravenous administration of sedative drugs is frequently used in conjunction with local anesthesia in a variety of dental procedures. Since sedation has come into popular use in dentistry, several agents have been introduced. Currently, techniques vary from using a single drug to using as many as a combination of four. The differences between the individual drugs as well as the rationale for using combinations of drugs has not been investigated adequately. Potential clinically significant differences between drugs may exist concerning such important parameters as peak sedation, duration of sedation, psychomotor performance, and memory. I propose to develop a model to evaluate drug effects on the above parameters. Various tests have been adapted or developed to evaluate simple motor coordination, complex psychomotor performance, short-term and long-term memory. A pilot study has been performed which demonstrated the preciseness and sensitivity of these tests. Subjects will be volunteers who normally would be receiving intravenous sedation for dental surgery. Subjects will be tested preoperatively and then postoperatively at 15 minutes, one hour, and then hourly for five more hours. Four 7-milliter blood samples will be taken over the six-hour test period and assayed for parent drug and metabolites in order to correlate plasma concentrations of drug with behavioral effects. The surgeon and research nurse will give a subjective evaluation of the quality of sedation. Once the model is established, my future plans are to compare the spectrum of drugs commonly used for intravenous sedation. Of particular interest, is the contribution of each constituent in combination treatments.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

10.0071, PSYCHOPHYSIOLOGICAL ASSESSMENT OF INTRAVENOUS SEDATION

R.A. Dionne, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, Anesthesiology Section, *9000 Rockville Pike, Bethesda, Maryland* 20205 (Z01 DE 00132-05 NA)

The purpose of this project is to systematically assess the physiological responses to drug combinations used to alleviate anxiety in dental outpatients. Cardiovascular and respiratory functions are monitored noninvasively by means of an impedance cardiograph, earpiece oximeter and automatic blood pressure recorder. Results of the project indicate that the combination of diazepam-fentanyl and methohexitol causes a decrease in stroke volume which is accompanied by a reflex tachycardia. This combination results in a decrease in arterial oxygen saturation. The use of diazepam alone and diazepam plus fentanyl does not result in any detectable cardiovascular or respiratory effects. The methodology employed in this study will be used to assess other intravenous, inhalational, and oral agents which can be useful for alleviateing pain and anxiety in dental outpatients.

BIBLIOGRAPHIC REFERENCES: Gelfman, S.S., Gracely, R.H., Driscoll, E.J., Wirdzek, P.R., Butler, D.P. and Sweet, J.B.: Comparison of recovery tests after intravenous sedation with diazepam-methohexitol and diazepam-methohexitol and fentanyl. J. Oral Surg., 37:391-397, 1979. Driscoll, E.J. and Gelfman, S.S.: Thrombophlebitis: Its Incidence and Natural History. J. Oral Surg., 37: In Press, 1979.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$112,057

DIAGNOSIS & TREATMENT - OTHER BEHAVIORAL SYNDROMES

10.0072, CHILDREN'S ACCEPTANCE OF CARIES PREVENTIVE PROCEDURES

S.S. Kegeles, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Behavioral Sciences & Community Health, *Farmington Ave., Farmington, Connecticut* 06032 (R01 DE 03868-05)

In the first experiments funded under this research program, we found that provision of contingent rewards increased children's acceptance of two preventive dental activities. In a third experiment, 501 seventh graders were asked to use an acidulated phosphate fluoride mouthrinse daily for 20 weeks at home, the same program used in the second experiment. Urban and suburban students were assigned to one of four persuasive conditions: (1) contingent rewards alone (CR); (2) CR and postcard reminders; (3) CR and action instuctions; (4) CR and postcard reminders and action instructions. Initial analyses indicate that action instructions increased the efficacy of contingent rewards for urban children, but either decreased or had no effect for suburban children.

A fourth experiment is underway in which 836 urban and suburban seventh graders were again asked to participate in a home mouthrinsing program. Based on findings from Experiment 3, action instructions were used with all children for increasing the return of signed parental consent forms. Two contingent reward conditions are being investigated: (1) small immediate rewards every two weeks plus a bonus reward for optimal behavior throughout the current reward program (CR); (2) small immediate rewards initially every two weeks but with a progressively thinner schedule. In each reward condition, half the children received instruction in behavioral self-management techniques while the other half did not. The reward procedures are discontinued after 14 weeks, while the children's participation will be monitored for a total of 40 weeks. As in the earlier experiments, analyses will be made of (1) experimental effects on acceptance of recommended procedures; and (2) demographic and attitudinal characteristics of children who accept or do not accept the procedures.

BIBLIOGRAPHIC REFERENCES: Lund, A.K., Kegeles, S.S. and Weisenberg, M. Motivational Techniques for Increasing Acceptance of Preventive Health Measures. Medical Care, Vol. XV, No. 8,p. 678-692, 1977. Kegeles, S.S., Lund, A., Weisenberg, M. Acceptance by Children of a Daily Home Mouthrinse Program. Social Science in Medicine, 12:199-209, 1978.

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U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$111,261

10.0073, BEHAVIORAL STAGES FOR CLEFT PALATE PATIENTS

P. Starr, Lancaster Cleft Palate Clinic, Dept. of Social Research, *24 N. Lime St., Lancaster, Pennsylvania* 17602 (R01 DE 04779-02)

We are now completing the first year of a longitudinal study of the behavioral functioning of patients with cleft lip and/or palate. Data will be collected from patients at two, four, six, ten, 15 years as well as young adults (24-30 years of age). Data will also be collected from appropriate comparison groups. They will be matched on age, sex, and socio-economic status. The kind of data collected will be familial, behavioral, and attitudinal. Discriminate analysis will be used to determine whether there is a significant difference and the nature of the difference between the two groups. At this time, we have completed the data collection for the two year olds and are collecting it for the other age groups. It is hoped that the behavioral comparisons for the patient and comparison group will serve as yard-sticks for clinicians in their treatment of patients.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$53,374

10.0074, PSYCHOLOGICAL IMPLICATIONS OF DENTOFACIAL MALOCCLUSION

L.W. Graber, University of Michigan, Ann Arbor Campus, Center for Human Growth & Development, *Ann Arbor, Michigan* 48104 (R01 DE 05095-01)

The proposed research first focuses on the problem of detection of malocclusion-- does the layman recognize a malocclusion when he sees one? If so, what aspects of the appearance differentiate the face from a normal face. The second part of the study will consider the attitude formulation phase of the observer of a malocclusion. It evaluates the formation of attitudes toward malocclusion for the individual with the characteristic, his family and society as a whole. The purpose of this series of studies is to examine the general esthetics of malocclusion in order to examine its impact on rated attractiveness and physiognomic stereotyping. Evaluations of personality and behavior patterns will be made in people with normal occlusions, treated and untreated malocclusions.

A diverse group of methodologies and instruments will be utilized to attack this multidisciplinary problem. Cephalometric and anthropometric evaluations of facial form will be related to a variety of social psychological data collected on dentofacially normal and abnormal subjects. This project addresses questions of practical significance in public health planning. Results from this research may have potential applications in setting parameters for orthodontic treatment provided under currently considered health care delivery systems.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$79,512

10.0075, BEHAVIORAL CONTROL OF BRUXISM

A.G. Glaros, Wayne State University, School of Liberal Arts, Dept. of Psychology, *4841 Cass Ave., Detroit, Michigan* 48202 (R23 DE 04536-03)

Bruxism, a non-functional gnashing or grinding of teeth, may be viewed as a learned response to arousal. The proposal here is to develop and evaluate a number of behaviorally based psychological treatments for bruxism. Subjects will be given a classical conditioning treatment for nocturnal bruxism or a biofeedback treatment for diurnal clenching.

BIBLIOGRAPHIC REFERENCES: Glaros, A.G. & Rao, S.M. Bruxism: A critical review. Psychological Bulletin, 1977, 84, 767-781. Reprinted in Der Zahnartz, 1978, 22, 91-97. Glaros, A.G. & Rao, S.M. Effects of bruxism: A review of the literature. Journal of Prosthetic Dentistry, 1977, 38, 149-151. Reprinted in Der Zahnartz, 1977, 21, 599-610.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

10.0076, CLINICAL TEST - PREVENTIVE DENTISTRY FOR THE AGED

A. Kiyak, University of Washington, School of Dentistry, Dept. of Community Dentistry, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (R23 DE 05235-01)

The proposed study is concerned with the oral health of elderly Americans. It aims to develop and compare the efficacy of programs in preventive dentistry for an institutionalized elderly population. The research will represent an initial effort to educate the elderly in oral hygiene and to monitor the success of such a program. The immediate and long-term effects of two different preventive education models will be compared with a periodic check-up and a control condition. Changes in oral hygiene habits, in status of oral health, and in self-sufficiency of oral care will be assessed in this longitudinal study. Finally, the psychological impact of improved oral hygiene and increased self-sufficiency will be investigated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$31,432

DIAGNOSIS & TREATMENT - DENTAL PAIN SYNDROMES

10.0077, PSYCHOPHYSIOLOGY OF TMJ & OTHER FACIAL PAIN SYNDROMES

D.M. Laskin, University of Illinois, Medical Center at Chicago, School of Dentistry, Dept. of Oral & Maxillofacial Surgery, *1853 W. Polk St., Chicago, Illinois* 60680 (R01 DE 02899-11)

This research program emphasizes the psychological and physiological factors in the etiology and treatment of myofacial pain-dysfunction (MFD) syndrome and the objective evaluation of various physical, pharmacological and psychological modalities used for the management of this condition. Historical, physical and psychological data on patients with other atypical facial pain syndromes are also being collected with the ultimate objective of analyzing many of the same factors that initially led to a better understanding of MPD syndrome. Investigations of organic temporomandibular joint disorders are also continuing since their etiology must be understood in order to establish a rational approach to prevention and cure.

BIBLIOGRAPHIC REFERENCES: 'Changes in Consistency of Occlusal Contact in Myofascial Pain-Dysfunction Syndrome.' Edmiston, G.F. and Laskin, D.M. J. Dent. Res. 57: No. 1, 27-30, 1978. 'Liquid Crystal Thermography in the Myofascial Pain-Dysfunction (MPD) Syndrome.' Apfel, M.S. and Laskin, D.M. J. Dent. Res. 57: Special Issue A, 92, 1978 (Abstract).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$84,598

10.0078, EXPERIMENTAL AND PERIODONTAL SURGICAL PAIN

G.M. Smith, Massachusetts General Hospital, Dept. of Anesthesia, *32 Fruit St., Boston, Massachusetts* 02114 (R01 DE 04939-02)

This project will study a method of producing graded levels of periodontal surgical pain, induced under controlled and standardized conditions, and will test the sensitivity and resolving power of that method both for discriminating known differences in analgesic potency and for studying the influence of personal variables on the pain response. A questionnaire will be developed to predict individual responses to pain by using self-report information concerning psychological characteristics. Stability of individual differences in tolerance for pain induced by each of our four procedures (periodontal, radiant heat, electric shock, and tourniquet) will be studied to clarify the status of pain tolerance as a possible general behavior trait; and the reliability and analytic resolving power of a multimethod approach that utilizes all four of those procedures for inducing pain will be tested. Subjects will be healthy college-age volunteers who are studied with questionnaires and with laboratory procedures for inducing and evaluating pain. Standard univariate and multivariate analytic procedures will be used to evaluate results.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$68,751

10.0079, PILOT STUDY FOR DENTAL SURGERY PATIENTS

F.H. Sarnquist, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Anesthesiology Service, *3801 Junipero Serra Blvd., Palo Alto, California* 94304 (640-008-F)

The purpose of this study was to evaluate the dental surgery population for the feasibility of establishing a program to evaluate new promising analgesic compounds.

In this pilot study we used standard analgesic drugs prescribed by the oral surgeon for the management of postoperative dental pain. The candidates for the study were selected by the oral surgeon and then interviewed by a research nurse-observer. The patient was informed of study procedures and signed an informed consent. He was asked to fill in a form evaluating his pain relief at hourly intervals after taking his prescribed medication and asked to return the form when he returned for his postsurgery examination.

It was the concensus opinion that the dental surgery population at the PAVAMC would be acceptable for a program involved in evaluating investigational analgesics or those compounds that are currently on the market but do not have FDA approval for package inserts for dental postoperative pain.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

10.0080, DESENSITIZATION OF TEETH

H.J. Aleff, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *W. Pleasant St., Knoxville, Iowa* 50138 (592-001-P)

Ninety-five sensitive teeth from 15 patients over age 40 were desensitized with either strontium fluoride, stannous fluoride, sodium fluoride or strontium fluoride prior to extraction for other reasons (caries and peridontitis). Results revealed no statistically significant reduction in tooth sensitivity between pretreament and one hour and one week post treatment nor between the four agents. Thirty-two teeth (43%) did show clinical improvement after desensitization indicating psychological parameters may override desensitizing physiochemical changes taking place in the tooth.

Mapping and concentration measurements of fluoride (F) were made at different parts of each extracted tooth. Teeth were dehydrated, embedded in Bioplast, sectioned transversely at root, polished and adapted to a computerized ARL electron probe for analysis of F. Automated transverse step-scans at 12 Kv with a 2 um beam were recorded from pulpal to enamel edges.

RESULTS INDICATE: 1) F levels decreased in an apico-coronal direction; 2) F levels were over 900 um at the pulpal edge as opposed to 400 um from the enamel or cemental edges; 3) enamel edge concentrations were higher than reports on levels in teeth of younger persons; 4) F was higher at or outside the roots than in the enamel edge; and 5) F fell below 700 ppm in several areas of the enamel edge.

The localization of F in older teeth lends support to the hypothesis that F may provide some caries protection. High F levels at the pulpal side indicated odontoblastic processes live in a high F environment.

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U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

10.0081, INTRAVENOUS SEDATION IN PERIODONTAL SURGERY

T.N. Sims, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-008-F)

Intravenous conscious sedation was utilized during 113 periodontal surgical procedures to determine the relative effectiveness of diazepam, meperidine, and D5W. Effectiveness was measured by quantifying the level of sedation, duration of sedation, degree and duration of amnesia, and the variation in vital signs. There were eight patient groups, determined by the level of sedation produced and whether meperidine and/or diazepam was administered. Blood pressure, pulse, and EKG tracing were monitored. After the surgery, patients were asked to identify common objects shown to them immediately, 15 and 30 minutes after the sedation.

The amount of diazepan administered ranged from 0.1 to 0.38 mg/kg, illustrating the need for titration. The average dose of meperidine was 32 mgs. Immediate post sedation amnesia was present in 67-100% of the patients whose sedation included diazepam. Meperidine, alone, caused no amnesia. However, meperidine, when administered in conjunction with diazepam, showed a tendency to increase amensia. Few patients were amnesic at 30 minutes past sedation.

Sedated patients experienced a reduction in systolic blood pressure of 12 mm. hg. and a 6mm. hg. reduction in the diatolic pressure. Diazepam and meperidine sedations had an increased duration when compared to diazepam only sedations.

Intravenous conscious sedation utilizing diazepam, meperidine, and a continuous D5W drip, was found to be a safe and effective method of relieving patient stress and anxiety during periodontal surgical procedures.

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U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

DIAGNOSIS & TREATMENT - ORAL-FACIAL PAIN SYNDROMES

10.0082, THE APPLICATION OF ELECTROANALGESIC CURRENT FOR RELIEF OF ORO-FACIAL PAIN

B.S. Savara, Oregon State Higher Education System, University of Oregon Health Sciences Center, School of Medicine, Dept. of Otology Rhinology & Laryngology, *3181 S.W. Sam Jackson Park Rd., Portland, Oregon* 97201 (DADA17-70-C-0075)

Develop a local electro-anesthesia method involving teeth and to produce limited analgesia in general operative procedures in dentistry. secondary objectives to determine efficacy of electric current in desensitizing tooth structure and determine the electrical stimulation can accelerate fracture healing. Equipment will be adapted for field use greatly reducing logistical requirements. The development of procedures that hasten fracture repair and wound healing is obviously pertinent because of direct contributions to increased personnel effectiveness. Finally, the accelerated treatment and resultant reduction in patient hospital/clinic time is a most important premium.

A modified neurodyne instrument will be used to produce a bidirectional rectangular pulse with high frequency 8k-10k and will be used with two sets of electrodes on primates. Deposition of electro-negative fluoride ions on tooth structure will be accomplished to determine desensitizing efficiency. Electrostimulation will be applied to line fractures and healing rates and stages compared against known healing rates and stages.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Care of the Wounded Div.	$54,817

10.0083, THE USE OF ELECTRIC CURRENT AS AN ANESTHETIC AGENT

E.F. Huget, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Dental Materials, *Washington, District of Columbia* 20314 (DA0E6037)

To develop effective electroanalgesia equipment and techniques for easier and safer management of 'anesthetic risk' patients requiring immediate and extensive treatment of combat injuries of the oral-facial region. The simplicity of technique and equipment make this method ideally suited for use in field medical surgical practice, in the treatment of large numbers of patients in mass casualty situations and in the fixed dental treatment facility. The success of this project will establish cost effective measures which will eventuate in vast dollar savings.

To construct equipment for the synthesis and delivery of electroanalgesic currents. This will be followed by studies designed to determine optimum currents and frequencies. Methods of application and administration through time and intensity changing currents and chemical adjuncts will be studied. The final study will involve a demonstration of the safety of the use of this equipment.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research	funds n.a.

10.0084, ORAL-FACIAL EVALUATION OF UNTREATED TRIGEMINAL NEURALGIA

P.J. Dyck, Mayo Foundation, *200 1st St. S.W., Rochester, Minnesota* 55901 (N01DE62497 (CONTRACT))

The contractor plans to establish whether an abnormality of cutaneous touch-pressure sensation, of pallesthesia, of thermal discrimination and of nociception can (or cannot) be demonstrated in trigeminal neuralgia and in atypical facial neuralgia; compare the type of abnormality of sensatation is found in trigeminal neuralgia and in atypical facial neuralgia; determine whether morphometric and pathologic methods, of Cr V nerve twigs and ganglion, morphologic abnormality can be demonstrated in trigeminal neuralgia.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$56,685

10.0085, STUDIES OF MAXILLOFACIAL PAIN MECHANISMS AND CONTROL - MICROSURGICAL CONTROL OF TRIGEMINAL PAIN

J.M. Gregg, University of North Carolina, Chapel Hill Campus, Dental Research Center, *Chapel Hill, North Carolina* 27514 (P50 DE 02668-130201)

A computer-assisted model for quantifying the severity of chronic clinical pain problems has been developed. It is used as a basis for diagnostic input by members of a multidisciplinary team and also to serve as a more objective basis for studies of pain mechanisms and potential therapies. The objectives of this phase of the overall project are to aid in the development of microsurgical techniques for the control of trigeminal pain through objective neurosensory evaluations. Laboratory animals will be used to improve the armamentaria and surgical techniques and to study the effects on peripheral trigeminal fiber spectra for acute nerve repair, microsurgical decompression, radiofrequency thermal and cryosurgical lesions. Effects on injured peripheral nerve structure and function will be studied using fiber spectrum analysis and horseradish peroxidase retrograde transport to trigeminal ganglion. In the clinical phase of this study similar nerve injuries, repairs and microsurgical lesions will be studied in patients using classical neurosensory threshold measures and psychophysical examinations in selected cases. The effects and relative merits of the specific microsurgical techniques in controlling traumatic pain and improving sensory function will be measured in order to set better guidelines for patient care.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$28,223

10.0086, TREATMENT OF TEMPOROMANDIBULAR JOINT PAIN

E.N. Gale, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Behavioral Sciences, *3435 Main St., Buffalo, New York* 14214 (R01 DE 04358-04)

X. PAIN CONTROL & BEHAVIORAL STUDIES

A major problem for dentistry has been the lack of effective treatment for long term temporomandibular joint pain. Many of the patients who report pain the temporomandibular area have been successfully treated, especially when therapy is initiated early in the disorder. There remains, however, a large group of patients who have remained relatively intractable to treatment. These patients, because of the continual pain, require an inordinate amount of time from the dental profession.

Past work by the principal investigator has shown the possibility of biofeedback relaxation treatment to be effective for temporomandibular joint pain. The proposed research will attempt to evaluate and extend the effectiveness of treatment. Attempts will be made to experimentally control various biofeedback and relaxation techniques. In addition, effects of motivation and involvement in treatment will be evaluated in relation to successful therapeutic intervention. Pain as muscular response and inhibition of pain as a relaxation response will be also investigated. Successful treatment of TMJ pain and the improvement in biofeedback methodology are the major goals of the present research proposal.

BIBLIOGRAPHIC REFERENCES: Gale, E. N. Psychological Characteristics of Long Term Female Temporomandibular Joint Pain Patients, Journal of Dental Research (in press for July, 1978).

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PREVENTION

10.0087, DENTAL CONFERENCE ON BEHAVIORAL/SOCIAL SCIENCES

H.L. Bailit, International Assn. for Dental Research, *211 E. Chicago Ave., Chicago, Illinois* 60611 (R13 DE 05319-01)

It is increasingly apparent that the solution of major oral health problems depends, in part, on persuading individuals and institutions to behave appropriately in terms of self care, utilization of professional services and allocation of resources. The proposed conference will focus on two related issues: (1) determining the psychological, social and financial impact of oral disease on individuals and populations and (2) influencing the oral health behavior of individuals.

For each topic, the conference objectives are to define the state of behavioral and social science knowledge, suggest research priorities and propose general research strategies. These objectives will be achieved by bringing together 40 grant-supported and 60 self-supported behavioral and social science investigators for a two-day national conference in Washington, D.C. The conference format will consist of four prepared papers, two prepared critiques of each paper and general discussions. All conference materials will be edited for publication as a supplement to the Journal of Dental Research and will be disseminated to both the dental and behavioral and social science research communities. Through the conference and resulting publication, major progress should be made in stimulating behavioral and social scientists to focus on the major problems related to improving the oral health of the American people.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Inst. of Dental
Research $47,625

XI. CLINICAL EVALUATIONS

EQUIPMENT/INSTRUMENTS/DEVICES

11.0001, DENTAL EQUIPMENT DEVELOPMENT AND EVALUATION FOR FLEET HEALTH CARE

J.C. Cecil, U.S. Dept. of Defense, Navy, Naval Dental Research Inst., Dept. of Clinical Investigation, *Great Lakes, Illinois* 60088 (DN977574)

TECHNICAL OBJECTIVE: The usual dental equipment commercially produced is suited for the private practice of dentistry, with perhaps or 3 operatories. In military serivices there are often group practice clinics with up to 100 operatories in one facility. There are also fleet and field situations where equipment is required for dental care, for which few manufacturers produce specific equipment. The objective is to evaluate dental equipment and devices and facility prototypes to develop innovations which will support unique requirements of naval dental operations afloat and in the field.

APPROACH: Promising dental equipment and facilities prototypes with sea-service applicability will be developed, refined and tested in response to projected military medical and dental support requirements of future and potential combat arenas. Anatomy and physiology will be applied with engineering principles to develop innovations useful, functional, efficient for operational conditions. Light weight, compact, rugged, durable and maintainable products will be clinically evaluated for service use before being recommended for procurement.

SUPPORTED BY

U.S. Dept. of Defense, Navy, Naval Medical Research & Development Command, National Naval Medical Center	funds n.a.

DRUGS

11.0002, ANESTHETIC EXPOSURE AND HEALTH OF DENTAL PERSONNEL

E.N. Cohen, Stanford University, School of Medicine, Dept. of Anesthesia, *Stanford, California* 94305 (R01 OH 00775-02)

Recent epidemiologic studies indicate that chronic exposure to inhalation anesthetic gases may have a deleterious effect on the health of personnel employed in the operating room. A comprehensive study of exposed personnel in the hospital operating rooms of this country was recently conducted by the American Society of Anesthesiologists for the National Institute for Occupational Health and reported in 1974. This major study confirmed the findings of previous small-scale studies, all of which indicated an increase in the rate of spontaneous abortion and birth defects in exposed operating room personnel. There was also a significant increase in the incidence of liver disease and unexpected disclosure of a higher rate of congenital anomalies in unexposed wives of practicing anesthesiologists. The belated suspicion that a large segment of the dental profession might be similarly affected was given support when a small pilot study of dentistry disclosed similar serious health hazards.

The purpose of the present investigation is to study in detail the health histories of dentists, their wives, and auxiliary personnel numbering nearly 100,000 individuals. A unique opportunity in this effort will be the study of a large occupational group exposed to a single agent, nitrous oxide, versus the anesthetic gas mixtures.

A two-phase questionnaire survey has been designed to first identify those dentists who use and those who do not use inhalation anesthetics. The investigation will then concentrate on the health hazards of the users, ther wives and exposed employees. In turn, this group will be compared to a control group of non-inhalation anesthetic users. A carefully designed written questionnaire, fashioned after that used in the original ASA-NIOSH survey of hospital operating room personnel. will be employed. The questionnaire will be followed by written and telephone communications, ensuring a high response rate and adding validity to the overall health findings.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health	$114,550

11.0003, EXPERIMENTAL DENTALLY RELATED ENDOCARDITIS

S.L. Bahn, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *W. Spring St., West Haven, Connecticut* 06516 (689-003-F)

The volunteer research assistants are now attending Medical Schools. Ten animals were cannulated into the aortic valve area and injected intraorally (into the palate) with Strep Mitis and an attempt was made to evaluate the efficancy of Ampicillin at varying dosages. Consistent complete prophylaxis in the test group was not seen. At the present time, we are collating the results for publication and do not plan further animal studies.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

11.0004, PHARMACOLOGY OF ACTH DERIVATIVES MEASURED ON ADRENAL TUMOR CELL CULTURES

L.J. Cuprak, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Togus, Maine* 04330 (402-001-P)

Three carboxy terminal analogs of porcine ACTH have been synthesized by methods previously reported and their homogeneity verified by high-voltage electrophoresis, Sephadex gel filtration and thin layer chromatography. The amino acid composition of the glycine methyl ester (GME) analog has been determined and the results indicate that only three GME residues have been added per mole of ACTH although six carboxy sites were available. It would appear, therefore, that the ACTH peptide has a secondary structure in which the remaining sites were sterically hindered under these reaction conditions which were not carried out in urea. The coupling reaction of ACTH and diaminopentane yielded two analog products, DAP I and DAP II. Preliminary evidence indicates both products to be biologically active. Log dose response curves established for the GME, galactosamine (GlcNH2) and the DAP I analog are characteristic of each and they all differ from that of the native peptide. The molar potency and intrinsic activity for each analog are to be estimated using steroid response and 3'-5' cyclic AMP (cAMP) determinations. Upon completion of the latter for the three analogs synthesized to date, additional analogs will be made to attempt to correlate the observed modulation of cell response to the alterations in the carboxy terminal portion of the peptide.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

MATERIALS

11.0005, WOUND DRESSING IN MAXILLO-FACIAL TRAUMA

D.L. Williams, Abcor Inc., Biomedical Division, *850 Main St., Wilmington, Massachusetts* 01887 (DAMD17 79 C 9020)

The objective of this study is to develop and evaluate medicated dressings containing antiseptic, anesthetic, anti-inflammatory and hemostatic agents. Seven medicaments (iodine, cetylpyridinium chloride, procaine, benzocaine, etidocaine, hydrocortisone, and epinephrine) will be incorporated with four biogradable polymers (poly-l)-)lactide, R.S.V. is equivalent to 0.3, 1.0, poly-dl-lactide, R.S.V. Equivalent to 0.3, and an R.S.V. Is approximately equal to 0.3 lactide/glycolide copolymer) in three physical forms (non-woven fabric, powder, and aerosol spray) for potential use in wound dressing.

Non-woven fabric will be prepared by spraying an appropriate drug/polymer solution (e.g. In methylene chloride) from an atomizer, onto a screen. This screen could be a cotton gauze in the final system. powders will be prepared by addition of a non-solvent to the drug/polymer solution, and pulverizing the resultant material. drug/polymer films will be sprayed as an aerosol for potential direct application to wounds. Release of these medicaments will be evaluated by diffusion into ditilled water, using redox titration (i sub 2) or uv analysis (other drugs). Those drug/polymer systems showing potential wound dressing appliction will be combined, as appropriate, with each other and with the hemostatic agents, avitener and sodium amylosuccinate. Consideration will be given to appropriate delivery systems, and potentially useful systems will be submitted to the Institute of Dental Research for in vivo evaluation.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command	$47,689

11.0006, PROBLEMS INVOLVED IN MILITARY ORAL HEALTH CARE DELIVERY RELATED TO THERAPEUTIC AGENTS AND MATERIALS

M.F. Grower, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Basic Sciences, *Washington, District of Columbia* 20012 (DA0D6021)

To evaluate the special military problems of drug storage, heat susceptibility, long-term drug potency, sterility of bulk items, lack of refrigeration in combat zones and delivery to the patient. To investigate drug hazards. To investigate the use of biodegradable polymers for the long-term, slow release delivery of drugs.

Experiments will be conducted to evaluate pain killing medicaments used in military dental practice. The hazards involved in the use of various drugs will be studied and improved means of drug delivery will be investigated.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research	funds n.a.

11.0007, DEVELOPMENT AND EVALUATION OF DENTAL MATERIALS AND MATERIEL FOR ARMY USE

E.F. Huget, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Dental Materials, *Washington, District of Columbia* 20314 (DA0G6033)

To evaluate new materials and materiel of special interest to the Army dentist. Criteria for selection of materials, devices or techniques for evaluation are based on anticipated high potentials for-(1) savings of fiscal and/or manpower resources- (2) work simplification- (3) improved health care delivery in combat areas- and (4) enhanced safety with respect to professional and ancillary personnel as well as to the patient.

New materials will be evaluated on the basis of the following parameters- composition, microstructure, physical and mechanical properties, cytotoxicity, and clinical performance.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research	funds n.a.

11.0008, STORAGE STABILITY OF MATERIALS OF INTEREST TO THE MILITARY DENTIST

E.F. Huget, U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research, *Washington, District of Columbia* 20012 (DA0G6047)

Among the most prominent problems in providing logistical support to the military dentist world wide are those related to the shipment and storage of certain dental materials. Climactic conditions ranging through tropical, arid and artic-like can have a profound effect on the properties and characteristics of such substances as organic-inorganic composites, waxes and elastomeric impression materials. The objective of this study is to develop reliable techniques for the assessment of the storage stability of a variety of dental materials so that the most suitable materials for application in the field environment can be identified.

A programmable, extended range, constant temperature/humidity cabinet will be used to evaluate the 'weatherability' of dental composite restoratives. Unopened 'as-received' packages of selected materials will be subjected to simulated storage conditions ranging from 10 to 90 days followed by conventional testing to determine the effects of those conditions on the properties and characteristics of the subject materials.

SUPPORTED BY
U.S. Dept. of Defense, Army,
Medical Research &
Development Command, Inst.
of Dental Research funds n.a.

11.0009, INDUCED OSTEOGENESIS IN CRANIOFACIAL DEFECTS USING A BIODEGRADABLE CERAMIC AUGMENTED WITH FREEZE-DRIED SPECIES SPECIFIC BONE POWDER

J.F. Nelson, U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research, *Washington, District of Columbia* 20012 (DA0G6048)

Avulsive wounds of the maxillofacial complex and cranial areas have long posed a problem in effective resolution. Autogenous bone grafts have been found to be more successful than bone substitutes but require a second procedure which complicates the process and increases patient morbidity. The purpose of the present study is to determine the effect of combining powdered homograft freeze-dried bone with powdered biodegradable ceramic on osteogenesis in a created defect in the rat calvaria.

Created defects in rat calvaria will be filled with either a powdered tricalcium phosphate ceramic, powdered freeze-dried bone from the same species of rat used in the experiment or a 50-50 combination of ceramic and bone powders. Controls will receive no filler material. osteogenesis over a 16 week period will be studied histologically.

SUPPORTED BY
U.S. Dept. of Defense, Army,
Medical Research &
Development Command, Inst.
of Dental Research funds n.a.

11.0010, AN INVESTIGATION INTO THE SUSPECTED MODULATING EFFECT OF TRICALCIUM PHOSPHATE ON BONE RESORPTION IN VITRO

C.E. Hawley, U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research, Division of Oral Biology, *Washington, District of Columbia* 20012 (DA0H6035)

Combat wounds of the maxillofacial area frequently involve the resorptive loss of osseous tissues. There is some evidence to indicate that phosphate produces an effect which is synergistic to the inhibitory effect of calcitonin on bone resorption. The objective of this study is to determine if tricalcium phosphate ceramic (TCP) which is used as a repairative modality in osseous tissues, also excerts a positive modulating effect on bone resorption in vitro.

An in vitro bioassay technique will be used to evaluate the effect of tricalcium phosphate ceramic on 45ca labeled fetal rat long bone cultures. Long bone explants will be cultured in the presence and absence of TCP and the quantitative release of 45Ca will be used as in index of bone resorption.

SUPPORTED BY
U.S. Dept. of Defense, Army,
Medical Research &
Development Command, Inst.
of Dental Research funds n.a.

11.0011, CHANGES IN SERUM PROTEIN AND LIPID COMPOSITION AS A RESULT OF EXPOSURE TO METHYL METHACRYLATE MONOMER

R.A. Miller, U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research, Division of Oral Biology, *Washington, District of Columbia* 20012 (DA0H6041)

Studies have suggested that the highly voatile monomer of methyl methoacrylate is toxic. The relatively high usage of methyl methacrylate both by dental laboratory personnel and in the operatory indicate that it may present a significant health hazard to dental personnel. Non-specific elevation of lipid content and reduced protein in the serum of rats has been described in the literature. The objective of this study is to determine the specific serum protein and lipid changes occuring in experimental animals as a result of exposure to the monomer both in liquid and vapor form. The data will be used as a basis for determining the possible requirement for future studies on dental personnel.

Liquid monomer will be injected subcutaneously in rats and blood obtained at sacrifice. Rats will also be subject to monomer vapor inhalation over a period of 4 weeks and blood will be obtained at sacrifice. Serum lipids will be quantitated by clinical chemical methods and HPLC. Serum proteins will be quantitated by isoelectric focusing.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research funds n.a.

11.0012, MANAGEMENT OF HARD TISSUE AVULSIVE WOUNDS AND OROFACIAL FRACTURES

L.G. McCoy, Battelle Memorial Inst., *505 King Ave., Columbus, Ohio* 43201 (DADA17-69-C-9118)

To develop and evaluate ceramics and ceramic-coated metals with the potential for performing the specific functions of a graft alloplast in maxillofacial avulsive bone wounds. Further, the materials are to have the requisite structural properties of bone and be within the levels imposed by the necessity of tissue compatibility. This program is designed to solve serious combat surgical problems encountered in handling hard tissue avulsion mandibular wounds, and drastically reduce patient morbidity. Bone grafting techniques requiring donor sites from the already severely wounded patient will be eliminated and lengthy hospitalization and healing time will be significantly reduced.

Composite ceramic materials will be developed with properties that approach the physical characteristics of bone and with a controlled porosity that will allow attachment through bone ingrowth. After new materials are developed they will be implanted in surgical avulsive wounds of primates. Ceramic-coated screws, pins and plates will be developed to initially fix the implants to the bone segments. In all cases biocompatibility will be thoroughly evaluated.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Medical Bioengineering Research & Development Lab. $58,915

11.0013, THE INTERACTIONS BETWEEN BIOMATERIALS AND TISSUES, ESPECIALLY IN RELATION TO DENTAL AND ORAL SURGERY

D.F. Williams, University of Liverpool, Dept. of Dental Sciences, *P.O. Box 147, Liverpool L69 3BX, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council $27,976

PROCEDURES - PROSTHODONTIC

11.0014, APPLICATION OF LASER TECHNOLOGY TO MAXILLOFACIAL WOUND DEBRIDEMENT AND PROSTHETIC REHABILITATION

J.C. Adrian, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Pathology, *Washington, District of Columbia* 20012 (DA0F6040)

To determine the feasibility of the application of laser technology to prosthetic rehabilitation and to maxillofacial wound debridement and treatment.

Energy levels, methods of contour and approximation of pontics to establish optimum weld patterns and strengths will be investigated. This will be accomplished first in a bench set-up and secondly in animals to establish feasibility and safety. Comparison of the response of different mucosal sites to CO sub 2 laser energy will be made. Evaluation of the response of bone to the CO sub 2 laser will be made. Laser vs. surgical debridement of contaminated wounds will be done. Laser sterilization of metal instruments will be evaluated.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research funds n.a.

11.0015, THE CLINICAL EVALUATION OF PATIENTS TREATED BY THE MODULAR DENTURE TECHNIQUE

R.P. Feller, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *11201 Benton St., Loma Linda, California* 92357 (605-002-I)

A prospective study has been initiated to determine whether partially prefabricated dentures offer an acceptable alternative to conventional dentures. 138 male veterans, edentulous for at least one year, 65 years of age or younger, and meeting health and suitability requirements, will be treated randomly with conventional dentures or with partially prefabricated dentures processed by reline or rebase (1/3 of patients in each group). Evaluations include patient's and evaluator's opinion of dentures, condition of supporting tissue, retention and stability of dentures, sagittal area measuements of residual alveolar ridges, centric occlusion, vertical dimension, masticatory performance, dimensional stability, and record of time and patient visits required for dentist and technician. Patients are recalled every 6 months during the test phase until 2 years of data have been collected on each patient. Personnel have been trained in data collection and partially prefabricated denture technique on 10 non-study subjects.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

11.0016, COMPARATIVE STRESS ANALYSIS OF MAXILLARY ANTERIOR FIXED PARTIAL DENTURES

H. Thayer, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-001-I)

The loss of four maxillary incisor teeth due to a variety of factors is a relatively common clinical finding. When replacing these teeth with a fixed partial denture, the choice between single abutments or double abutments is generally made empirically. There is little scientific data to aid the clinician in making the decision. A photoelastic investigation of four maxillary anterior fixed partial dentures which vary both in the number of abutments and the length of the lever arm will be conducted to visualize the stresses produced in the supporting structures of the abutments when loads are applied.

The photoelastic model will be constructed using three different photoelastic materials. Initially, two single abutted fixed partial dentures with 3mm. or 6mm. lever arms, respectively, will be constructed and tested. The straining frame used to apply the load to the prostheses is constructed to fit into a circular transmission polariscope. The loaded photoelastic model will be able to rotate between a fixed light source and camera. Results will be photographed using high speed Ektachrome film (ASA 160).

After testing the single-abutted prostheses, the bicuspids will be prepared for full cast crowns which will subsequently be soldered to the cuspid full cast crowns. The double abutted prostheses will then be loaded and photographed.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

11.0017, SUBMERGED VITAL ROOT RETENTION ASSOCIATED WITH DENTURE PROSTHESES

L.O. Wible, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *1030 Jefferson Ave., Memphis, Tennessee* 38104 (614-001-I)

Patients who are scheduled to have all their remaining teeth extracted and dentures constructed will be given the opportunity to save the roots of selected remaining teeth. Over a period of twenty-four months, twenty-five patients will be evaluated as to the amount of bone lost and health of soft tissue associated with submerged roots after dentures are made.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

11.0018, ADVANCED RETENTIVE STABILIZING (RS) APPLIANCE DESIGNS - ENLARGE ROLE OF BASIC COMPONENTS

H.H. Berry, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Marion, Indiana* 46952 (610-002-F)

To date, seven retentive stabilizing appliances have been constructed using conventional designs for major assembly units and interrupted stabilizing arms. In addition, one RS appliance has been constructed using a modified (buccal) major assembly unit design to compare its effectiveness with the lingual placement of this component. RS appliance principles and concepts were also used in the construction of an appliances which were functioning successfully could only be achieved for the two latter mentioned patients.

As revealed by the smaller number (9) of RS appliances constructed over the past year, several presently existing conditions beyond the investigators control were not present when the project began.

The patient's hospital stay has been reduced from three months or more to one month or less which doesn't provide enough time for oral preparation and appliance construction.

Recall of patients to evaluate applicance performance is virtually impossible due to an ever increasing mobility of the veteran patient.

These facts give the investigator no alternative but to terminate the research project with this progress report.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

11.0019, EFFECT OF DENTURES ON BONE REMODELING, PHASE I

J.E. House, U.S. Veterans Admin., Dept. of Medicine & Surgery, Outpatient Clinic, Dental Service, *17 Court St., Boston, Massachusetts* 02108 (750-002-P)

Progress for this study has followed the timetable set initially. Location of volunteers to be examined at the Veterans Administration Outpatient Clinic consisted of retrospective review of thousands of dental charts of formally treated veterans. Those having received treatment that included completed upper and lower denture construction were listed. Letters of explanation/inquiry were mailed to 185 complete denture wearers. 50 positive responses of interest to participate were received. 33 volunteers were selected for the study. To date 20 of the hoped for total of 40 subjects have been examined. This progress is as targeted.

The 'feasibility' portion of this study includes subjects examined at the outpatient clinic as well as another group of subjects at Tufts University School of Dental Medicine. Seven subjects have been selected at Tufts and this completes our targeted 40 subjects.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

11.0020, DETERMINATION OF THE OCCLUSION PLANE IN COMPLETE PROSTHESIS

R. Sanguiolo, Universite dAix Marseille, Faculte de Chirurgie Dentaire, Dept. of Prosthetics, *Charles Livon Blvd., Jardin Emile Duclaux, 13007 Marseille, France*

Since 1977, the Department of Complete Prosthesis has been directed towards the study of determination of the occlusion plane in complete prosthesis based on geometrical, anatomical, physiological and teleradiographical data.

After an exhaustive schedule concerning the already published works on the subject, the Department has decided to carry out teleradiographical experiments on 500 cases.

SUPPORTED BY

Universite dAix Marseille	funds n.a.

PROCEDURES - RADIOGRAPHIC

11.0021, ERYTHROID EFFECTS OF RADIATION IN THE 1.0 R RANGE

J.K. Gong, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Biology, *3435 Main St., Buffalo, New York* 14214 (R01 FD 00800-03)

Last year (Sept. 1976 - Dec. 1977) we reported that single exposures of 50 mR X-rays consistently resulted in no abnormal levels of marrow nucleated red cells (RBCp) contents in terms of RBCp%, RBCp/whole femur or RBCp/skeleton when animals were five through 30 weeks post X-irradiation. Animals exposed to 150 mR or higher (550, 770 or 1500mR), on the other hand invariably demonstrated marrow erythroid alterations. In the present report (Dec. 1977 - present) it was found that 'subthreshold' dosages (25 or 50 mR) when employed two or more times within a seven day period consistently yielded alterative normoblastic changes when the summated dosages exceeded 100 mR. The findings suggest our 'subthreshold' dosages, so-called because no measurable effects could be observed following single exposures, could in fact, elicit changes which are too small to be measured. When the marrow is irradiated repeatedly, these subliminal effects are summated and measurable marrow effects are then detected. This phenomenon will be further studied during the next report period using intervals between acute subthreshold dosages of weeks to months. The goal will be to find an interval sufficiently prolonged that the subthreshold effects can no longer be summated to a level detectable by our animal model. Other studies to be included in the next year will involve further work on the low-dose X-ray effects on the splenic colonies of subralethally irradiated mice, a study of the possible pathologic effects triggered by phlebotomy in rats previously exposed to low-dose X-rays, as well as a study on the effects of chronic exposure with low dose-rate Cs-137 gamma radiation.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, Food & Drug Admin.	$47,663

11.0022, UTILITY OF PANORAMIC X-RAY EXAMINATIONS

S.C. White, University of California, Los Angeles Campus, School of Dentistry, Dept. of Oral Radiology, *405 Hilgard Ave., Los Angeles, California* 90024 (R01 FD 01036-01)

The primary objective of this proposal is to evaluate the influence of the use of referral criteria on the diagnostic yield of panoramic radiographic examinations of the oral structures. Data will be gathered from a general dental clinic, a pediatric dental clinic, and from an oral surgery clinic pertaining to the clinical indications used for ordering panoramic radiographs. The diagnostic yield from these examinations will be determined and correlated with the referral criteria employed and patient demographic data. This information will be used to construct high-yield referral criteria lists to identify those groups of patients who have a high yield of positive panoramic findings, as well as those patients for whom there is little expectation of benefit from panoramic radiography.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, Food & Drug Admin., Bureau of Radiological Health	$46,715

11.0023, A QUALITY CONTROL SYSTEM FOR DENTAL RADIOLOGY

J.D. Allison, Medical College of Georgia, School of Medicine, Dept. of Radiology, *1459 Gwinnett St., Augusta, Georgia* 30902 (R01 FD 01057-01)

A simple, inexpensive system for quality control of dental radiographs will be developed. The system will be easily implemented by dentists and dental ancillaries. Studies have shown that many dental radiographs are improperly processed and/or overexposed. Film used in dental radiology is low speed and has broad latitude. Because of the film characteristics, it is possible to obtain a usable diagnostic image over a wide range of processing and exposure conditions. The availability of viable quality control program for dental radiology can significantly reduce the genetic and somatic radiation exposure of the patient and help maintain exposures as low as reasonably achievable.

The principles of existing quality control programs for diagnostic radiology will be extended to dental radiology. The quality control program would function as follows: 1) Establishment and maintenance of good processing technique by proper initial set up and subsequent parameter charting 2) Determination of the minimum exposure necessary for an acceptable radiograph.

In order to produce a viable system, the research will proceed as follows: 1) The system will utilize the dental X-ray machine to produce optical density differences on a film, that are independent of the X-ray machine output. Optical densities will be determined using visual comparison to finely graduated step tablets. Charted parameters will be used to compare existing conditions to properly initialized conditions, detect change and then indicate appropriate corrective actions. A dental tissue phantom (or radiographic equivalent) will be used to determine the minimum exposure required for a useful diagnostic image. Concise instructions for system operation will be developed. 2) The system will be tested at 8 facilities, representing a spectrum of equipment currently in existance. System effectiveness will be evaluated for each facility. 3) Appropriate modifications will be incorporated into the system. 4) The production cost of the system will be estimated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, Food & Drug Admin., Bureau of Radiological Health	$28,728

11.0024, QUALITY CONTROL FOR DENTAL RADIOGRAPHS

R.G. Gould, University of California, San Francisco Campus, School of Medicine, Dept. of Radiology, *551 Parnassus Ave., San Francisco, California* 94122 (R01 FD 01065-01)

The objective of this proposal is to develop a reliable, simple and inexpensive quality control (QC) system for radiography in dental facilities. The proposed system will differentiate between exposure problems and changes in the processing conditions by testing each of these areas separately. The QC program will be applicable to both manual and automatic film processing. The x-ray equipment will be monitored by radiographing a test object under strict exposure and geometric conditions. To test the processing conditions, we propose to construct an inexpensive sensitometer which will use an electroluminescent panel to expose dental film to a graded series of light intensities. Problems with either the equipment or developing will be detected by comparing the film of the test object and the sensitometric film to appropriate reference films. A manual will be written to guide the user of the quality control program through the QC procedure and to help the user identify specific problems. The effectiveness and ease of operation of the QC program will be tested in the laboratory and in eight different dental facilities.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, Food & Drug Admin., Bureau of Radiological Health	$39,235

PROCEDURES - SURGICAL

11.0025, CRYOHEMOSTASIS - THE EFFECTS OF COLD ON BLEEDING

S.L. Bahn, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *W. Spring St., West Haven, Connecticut* 06516 (689-005-I)

Despite the universal application of cold to control hemorrhage by the laymen and numerous references in the medical literature recommending this procedure, we could find no experimental evidence to support this practice. We shall attempt to evaluate whether non-freezing cold is an effective hemostatic agent in mammalian tissue and define the optimum parameters (time and temp) for this effect. Standardized surgical wounds made in the rabbit ear will be monitored by recording bleeding times, coagulation time and intensity of blood flow at temperatures from ambient to 1 degree C. Temperature modification will be provided by a nitrous oxide drive cryogenic probe, with thermocouple control of probe and skin temperatures.

If non-freezing cold application can enhance hemostasis, at a definite time and temperature range, the treatment of operative and postoperative surgical bleeding, the control of hemorrhage in the anticoagulated patient or those with bleeding disorders, and emergency control of traumatic or neoplastic hemorrhage may be enhanced.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery funds n.a.

11.0026, MANDIBULAR RECONSTRUCTION WITH AUTOGENOUS MANDIBLE AND PEROSTEAL GRAFT

D.H. Rice, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Head & Neck Surgery Section, *Wilshire & Sawtelle Blvds., Room 209, Los Angeles, California* 90073 (691-003-I)

This project is an attempt to develop a better method of mandibular reconstruction. The diseased mandible will be removed, autoclaved, and re-implanted. The laboratory model will be dogs. The ends of the transected mandible will be covered with free periosteal grafts to promote osteoneogenesis. Mandibular segments will be removed from dogs, autoclaved, re-implanted, and immobilized. The dogs will then be followed and the formation of a new, viable, mandibular segment assessed.

This author has done prior work with the formation of a new cartilage from periochondrial grafts in the subglottis. This was successful in correcting subglottic stenosis.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery funds n.a.

11.0027, THE EFFECT OF DIFFERENT FLAP ELEVATION PERIODS ON BONE RESORPTION

T.E. Klag, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Leavenworth, Kansas* 66048 (686-001-I)

PURPOSE: To examine what effects different flap elevation periods of a mucoperiosteal flap will have on crestal bone loss in the premolar segments of mongrel dogs.

MATERIALS AND METHODS: Eight mongrel dogs will be randomly assigned to surgical treatment groups. I.V. Sodium Pentobarbital will be used to achieve anesthesia. A dental burr will be used to mark five points; mesial, mesial root, furca, distal root, distal, on the selected premolar tooth. A mucoperiosteal flap will be elevated and distances from the reference points to crestal bone will be recorded. The flaps will remain elevated for 0, 15, 30, and 60 min. The flaps will then be sutured in place.

Seven days post surgically the dogs will be sacrificed and post surgical crestal bone height determinations will be recorded in a manner similar to the surgical levels.

RESULTS: The data will be assembled in graphic form comparing bone loss at the J sites compared to time of flap elevation.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery funds n.a.

11.0028, DRY SOCKET FOLLOWING TOOTH EXTRACTION

B.A. Warren, University of Western Ontario, Health Sciences Centre, *1151 Richmond St., London, Ontario, Canada* N6A 5C1 (PR 686)

The objective is to determine the nature of the abnormality in dry socket following tooth extraction and the ways in which it can be averted.

APPROACH AND CURRENT PLANS: (a) The morphology of the blood clot that forms in the tooth socket will be compared with that formed in vitro by means of light microscopy, transmission and scanning electron microscopy. The clots from the sockets will be both animal (the rat) and human in origin. (b) The agents which influence fibrinolysis will be correlated with the morphology of the socket clot in normal and cases of dry socket. (c) The nature of the healing process when the blood coagulum is bathed in saliva and when it is inserted into the tissues will be compared in rats. Aspects of the stability of similar blood clots in these two locations will be studied in rats. (d) Different bacterial isolates from human subgingival and socket deposits will be examined for their effects on blood coagulum stability and fibrinolysis. (e) The effects will be compared of the healing of extraction wounds in the rat model following implantation of human subgingival or socket bacterial deposits with the normal process. (f) The presurgical saliva and subgingival bacterial flora will be compared with the postsurgical socket blood clot in cases in which normal healing has occurred and cases in which dry socket has developed. (g) The incidence of dry socket following various treatments of the gingival crevice prior to removal of isolated teeth will be compared with that occurring following normal routine extraction.

SUPPORTED BY

Ontario Provincial Government	$31,472

PROCEDURES - OTHER PROCEDURES

11.0029, THE MOLECULAR MECHANISM OF CYTOKINESIS - STRUCTURAL ASPECTS

R. Niederman, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *1400 Vet. of Foreign Wars Pkwy, West Roxbury, Massachusetts* 02132 (690-002-P)

The objective of study is to isolate and characterize the structure of myosin filaments.

Native myosin filaments were isolated from rabbit psoas using the method of Craig (J Mol Biol 109:69). A-segments were separated from individual myosin filaments by sedimentation at 1g. for one hour. Electron micrographs of negatively stained preparations revealed 1.6 micron long filaments with a dense staining area in the center of the bare zone. The dense area consisted of three transverse bands, and had a length and width of 50 and 30nm respectively. SDS-PAGE displayed bands that comigrated with myosin, actin, troponin, and tropo-myosin. In addition, bands of 170K, 160K, 150K, 115K, 105K, and 40K were noted.

Isolated filaments were dialyzed against .1M KCl, 1mM MgCl2, 20mM phosphate, pH 8. Under these conditions the filaments partially depolymerized forming mini-myosin filaments with filament and bare zone lengths of 417 nm plus or minus 52 (n equals 36), and 217nm plus or minus 28 (n equals 33) respectively. The center of the bare zone retained the 50nm x 30nm dense region with three transverse bands. Dialized filaments were spun at 3000g. for five minutes. As determined by SDS-PAGE the supernate had major bands at 115K, 105K, and 42K daltons while while the pellet had major bands at 200K, and 40k daltons.

These results support a model for the M-bridge (Knappies and Carlson, J Cell Biol 38:202) where M1 and M4 (Sjostrom and Squire, J Mol Biol 109:49; and Luther and Squire, J Mol Biol 125:313) are both 40K dalton proteins (Wallimann et al, J Cell Biol 75:297). The results also suggest that the M-band may function to stabilize the filament structure.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

11.0030, BLOTTING ROOT CANALS TO REMOVE MEDICAMENT BEFORE TAKING CULTURE (HUMAN)

E.I. Fuentes, Howard University, Graduate School, *2400 6th St. N.W., Washington, District of Columbia* 20001 (S06 RR 08016-090008)

This project is part of a broader program (RR 08016-09) whose summary states: A renewal application is made for continued minority Biomedical support for the Biomedical Interdisciplinary Project at Howard University. It consists of individual research elements with biomedical relevance and requests for support of strong undergraduate and graduate student research participation. The subject areas of Botany, Chemistry, Dentistry, Immunology, Psychology and Zoology are represented among 19 research project elements organized by individual faculty members or collaboratively among faculty in two or more disciplines.

Support is requested for visiting scientists to serve as a part of a Seminar-Science Conference component designed to promote University-wide communication among faculty and student scientists at Howard.

Overall, a program is proposed which will ultimately increase the biomedical research potential at Howard and add to the pool of minorities trained and prepared to perform at a high level in biomedical research.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, Div. of Research Resources	funds n.a.

11.0031, PREVENTING ORAL INFECTION DURING ANTINEOPLASTIC CHEMOTHERAPY

S.A. Dugan, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Hematology Oncology Clinic, *508 Fulton St., Durham, North Carolina* 27705 (558-002-P)

The purpose of this pilot study was to answer the question 'Will specific program of self-administered oral hygiene lessen the risk for developing secondary oral infections during antineoplastic chemotherapy?'

Thirteen patients were observed. Six patients in the experimental group did not develop secondary oral infections while their performance status remained 70 percent or above and they compulsively carried out the prescribed oral hygiene. Three patients (3 of 7) in the control group developed infections requiring therapy with antifungal oral agents. It appears that a specific program of self-administered oral hygiene did lessen the risk of secondary oral infections during chemotherapy.

It is recommended that the study be continued with the following modifications; 1) an evaluation of oral health be made on all patients receiving chemotherapy, and 2) all patients henceforth be instructed in the oral hygiene procedure as planned for this study.

The purpose of the continuing study will be to examine the relationship between oral health levels, the conditions of moistness, inflammation, ulceration, pain and the occurence of oral infections.

SUPPORTED BY

U.S. Veterans Admin., Dept. of Medicine & Surgery	funds n.a.

11.0032, DEVELOPMENT OF SIMPLE ECONOMICAL SPACE MAINTAINER

K.A. Galil, University of Western Ontario, Health Sciences Centre, Dept. of Anatomy, *1151 Richmond St., London, Ontario, Canada* N6A 5C1

The objective of this research is to introduce an economical and efficient space maintainer appliance which is easily applied to children's teeth and which will stay in the mouth for prolonged periods. The first part of the project is a laboratory study dealing with acid etchings of enamel and using the scanning electron microscope. The second part of the project deals with the clinical application based on the results of the first part.

SUPPORTED BY

Ontario Provincial Government	funds n.a.

OTHER CLINICAL EVALUATIONS

11.0033, IDENTIFICATION AND CONTROL OF ORO-FACIAL INFECTIONS OF MILITARY IMPORTANCE

A. Gross, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Basic Sciences, *Washington, District of Columbia* 20012 (DA0F6024)

To investigate the source and treatment of oro-facial infections encountered in field conditions, foreign countries and diverse climates; and to evaluate the special agents, instruments and chemicals necessary under military conditions.

Oro-facial infections of significance in the diverse military environment will be studied by microbiological, immunological and electron-microscopy methods. Possible sources of oral infections will be evaluated and the effectiveness of commercially available as well as in-house designs will be studied for their ability to control or prevent oral infections.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research	funds n.a.

11.0034, DEVELOPMENT OF TECHNIQUES FOR DETERMINATION OF CONCENTRATION OF INORGANIC NICKEL & OTHER PARTICULATE POLLUTANTS IN ARMY DENTAL LABS

E.F. Huget, U.S. Dept. of Defense, Army, Medical Research & Development Command, Div. of Dental Materials, *Washington, District of Columbia* 20314 (DA0G6045)

To establish within USAIDR the capability to monitor and to measure the concentration of nickel and other particulate pollutants in Army dental laboratories.

Airborne particulate matter will be collected from a metal-finishing room for a period of 35 days. Dust acquired from 5 intramural locations will be analyzed quantitatively for nickel content.

SUPPORTED BY

U.S. Dept. of Defense, Army, Medical Research & Development Command, Inst. of Dental Research	funds n.a.

11.0035, MERCURY BURDEN, HEALTH IMPAIRMENT IN DENTAL AUXILIARIES

I. Shapiro, University of Pennsylvania, School of Dental Medicine, Dept. of Biochemistry, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (R01 OH 00886-01)

Previous studies of dental personnel have indicated that mercury exposure in the dental office represents a health hazard of dental practice. Attempts to measure the clinical health deficits associated with exposure have been few. Furthermore, the investigations that have been performed have been limited to evaluating current mercury exposure through blood, urine or hair analysis. The important relationship between cumulative mercury exposure and chronic health impairment has not been studied. This research proposal addresses itself to examining this relationship.

The population consists of 300 dental auxiliaries who have had contact with mercury and a cohort of 50 dental auxiliaries who do not use mercury in their practice. Cumulative mercury levels will be ascertained by measuring bone and brain mercury levels in situ by an X-ray fluorescence technique that was developed in our laboratories. The top ten percent of the ranked population will then be further examined for neurological and renal deficits. Electrodiagnostic studies will measure nerve conduction velocity, denervation, neuromuscular transmission and sensory action potentials. Renal examination will include kidney urinary concentrating function, osmolality and urinary microprotein. The kidney mercury level will also be ascertained by X-ray fluorescence in the group demonstrating elevated bone mercury. Neuropsychological evaluation is being performed on the ranked upper and lower twenty-five percent of the population. A battery of eleven tests is being used. These comprise the Weschler Adult Intelligence Scale, Bender Motor Gestalt Test, Finger Tapping Test, Disjunctive Reaction Time Manual Dexterity Test, Vertical and Horizontal Groove Steadiness Test, Static Steadiness Test, Resting Steadiness Test, Purdue Pegboard Test, Grooved Pegboard Test, and the SCL Personality Test and the SCL Personality Inventory. Current mercury exposure levels of these populations will also be determined through analysis of blood, urine and hair and correlated with total body mercury burden as determined by X-ray fluorescence. The results of these evaluations will indicate whether functional health deficits have occurred as a result of mercury accumulation.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, Center for Disease Control, National Inst. for Occupational Safety & Health	$192,449

11.0036, GENERAL CLINICAL RESARCH CENTER DENTAL MEDICINE

D.W. Cohen, University of Pennsylvania, School of Dental Medicine, Dept. of Periodontics, *4001 Spruce St., Philadelphia, Pennsylvania* 19104 (M01 RR 01224-01)

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, Div. of Research Resources	$53,150

11.0037, SYNERGISTIC BACTERICIDAL ACTIVITY OF ULTRASONICS, ULTRAVIOLET LIGHT AND HYDROGEN PEROXIDE

M.L. Fuesting, Southern Illinois University, Edwardsville Campus, School of Dental Medicine, *Edwardsville, Illinois* 62025

The combined bactericidal activity of ultrasonic cavitation, ultraviolet irradiation and hydrogen peroxide was tested with a Bacillus subtilis spore suspension. A rapid 99 per cent bactericidal activity was proposed as a result of the synergistic effect of three agents. The spore suspension (10 to the sixth power/ml) was subjected to ultrasonic cavitation (240 watts, 52 KHz), ultraviolet irradiation (100 uW/sq. cm.) and H202 (6%) individually, in combinations of two and all three. After exposure, the spores were incubated at 37 degrees C for a week and counted. Fifteen minute exposure to ultrasonic cavitation (US) produced to kill and H2O2 alone produced less than a 90 per cent kill. The same exposure of the spores to ultraviolet irradiation (UV) and H2O2 or to US and H2O2 resulted in approximately a 90 per cent kill. The combination of UV and US or UV alone demonstrated a 99.9 percent bactericidal activity. The triple combination showed only a 90 percent kill, suggesting that H2O2 is blocking in the synergistic combination. The investigation is continuing and is centered on overcoming the blocking action played on hydrogen peroxide.

SUPPORTED BY

Southern Illinois University	$1,500

XII. DENTAL ANTHROPOLOGY/FORENSIC DENTISTRY

12.0001, COMMUNITY CARIES PREVENTION DEMONSTRATION PROJECT

B. Krippene, State Dept. of Health & Social Services, *1 W. Wilson St., Room 565, Madison, Wisconsin* 53702 (N01DE52465 (CONTRACT))

Briefly, the Contractor shall establish and conduct a school based caries prevention demonstration program; collect and report data on the cost and effectiveness of the program; and develop plans for continuation of the program after the expiration of Federal support. The preventive regimen shall consist of weekly fluoride mouthrinsing with 0.2%

solution of sodium fluoride. Grades K-6 or K-8 will be treated. If K-6 are treated, K-9 will be examined each year. If K-8 are treated, K-11 will be examined. DMF tooth and surface data shall be determined with mirror and explorer. Radiographs will not be used. Costs and staff time for implementing and conducting the project will be recorded. The Contractor shall also exert every effort to obtain funding from the community for continuation of the project for a period of three-years after the Federal support has terminated.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$0

12.0002, EVOLUTION OF TOOTH FUNCTION AND CRANIOFACIAL FORM

M.H. Wolpoff, University of Michigan, Ann Arbor Campus, School of Literature Science & the Arts, Dept. of Anthropology, *Ann Arbor, Michigan* 48104 (BNS76-82729 A01)

This research will focus on the evolutionary changes which have occurred in the human masticatory apparatus. Observations on tooth size, shape, morphology, pathology, wear and differential survivorship will be used to determine patterns of selections acting on the dentition, as well as changes in function. Other observations will be made on the size and form of the jaws, facial region, and parts of the skull. Skeletal remains from recent human and primate populations will be compared with fossil specimens now housed in the museums of various countries. Not only will this contribute new and important insights on the process of evolution of this portion of the anatomy, but it will provide a framework for analyzing developmental malformations in the dento-facial structures of living humans.

SUPPORTED BY

U.S. National Science Foundation, Directorate for Biological Behavioral & Social Sciences, Div. of Behavioral & Neural Sciences	$0

12.0003, DENTAL ATTRITION AND OCCLUSION IN VARYING ENVIRONMENTS

S. Molnar, Washington University, School of Arts & Sciences, Dept. of Anthropology, *4559 Scott Ave., St. Louis, Missouri* 63130 (BNS79-06859)

This project will involve the examination of the dental remains of several major Australian Aborigine skeletal collections and dental casts made from living Aborigines. The skeletons are of prehistoric age and span several thousand years. The casts are made from full mouth impressions taken from semi-acculturated Aborigines over a twenty year period and thus provide a record of the rate of change in dental attrition as the population increased their dependence on European foods. During the first year, records will be made of attrition, dental pathology, and supporting bone morphology. Radiographs and undecalcified thin sections will be made of selected specimens. These data will be analyzed during the second year to establish models to demonstrate the interrelationships of several variables which influence occlusal loading and attrition. The result of this project should provide insight into environmental influences on dentition and supporting structures and their responses over time and will lead to a clearer understanding of hominid evolution.

SUPPORTED BY

U.S. National Science Foundation, Directorate for Biological Behavioral & Social Sciences, Div. of Behavioral & Neural Sciences	$86,000

12.0004, THE ORIGIN OF THE FIRST AMERICANS - THE DENTAL EVIDENCE

C.G. Turner, Arizona State University, School of Liberal Arts, Dept. of Anthropology, *Tempe, Arizona* 85281

This proposal has two first order objectives. First, it is to prepare the way for intensive research in the USSR by personally meeting Soviet scientists attending the 14th Pacific Science Congress from August 20 to September 5, 1979, in Khabarovsk, eastern Siberia. Permission will be requested of these scientists for me to return in 1980 to examine their collections of historic and prehistoric human skeletons and teeth relative to my presently aided National Geographic Society study on the origin of the first Americans and to visit any possible early man sites in Siberia.

Second, this is a request for second year support for the computer data-processing student assistant I have helping me in the analysis of 515,000 observations from greater than 1800 American Indian & Aleut-Eskimo dentitions studied between June 4 to August 20, 1978. By May 31, the end of the 1978-79 NGS grant period, I expect to have completed another set of dental observations (286 possible per skeleton) on a 1000 plus American Indian collection at the University of Arizona, Tucson. NGS funds will carry the student assistant throught the summer on full time basis. A revised estimate shows, however, that card punching and checks are ca. 50% slower than estimated so analysis for 1978-79 is behind schedule. Needless to say, the student assistant is essential if this large number of variables (15 IBM cards/individual) is to be studied.

In addition, while in Vancouver, Japan, and Khabarovsk, I will try to locate and study any early man dental remains available.

SUPPORTED BY

National Geographic Society	$8,045

12.0005, CRANIOFACIAL GROWTH STUDIES OF AUSTRALIAN ABORIGINALS

T. Brown, University of Adelaide, Dept. of Restorative Dentistry, *P.O. Box 498, Adelaide, S. Australia 5001, Australia*

PURPOSE: To correlate morphological characteristics, functional relations, and patterns of growth and development from childhood through adolescence to young adulthood; and to study genetic family variation in metric characters of the dentition.

SUBJECTS: Children of pure Aboriginal ancestry, ages 6 to 20. 1,717 sets of dental casts were made for 446 boys and girls; and 1,160 sets of skull roentgenograms, for 250 boys and girls.

METHODS: Field visits to Central Australia were made each year from 1961 to 1971. Semiautomatic methods of date recording, using electronic digitizing instruments, have been developed to obtain measurements from dental casts and skull roentgenograms. Genealogical records and somatometric data were also obtained. Multivariate analysis of data has included factor analysis, discriminant function, and intraclass correlation methods.

FINDINGS: Reports have been concerned with metric characters of the dentition, skeletal maturation, the timing and sequence of tooth emergence, craniofacial morphology and growth, and general body growth. Growth standards have been developed for Australian Aboriginals.

SUPPORTED BY

(No Supporting Organization Reported)	funds n.a.

XIII. DENTAL CARE & PRACTICE

13.0001, PRELIMINARY EVALUATION OF NEW DENTAL MATERIALS, EQUIPMENT, DRUGS, AND PROCEDURES FOR NAVAL DENTISTRY

G.B. Pelleu, U.S. Dept. of Defense, Navy, Naval Graduate Dental School, National Naval Dental Center, *Bethesda, Maryland* 20014 (DN940223)

OBJECTIVE: To conduct preliminary and complete studies, under controlled conditions, of new dental materials, equipment, drugs, and procedures in treatmet of dental problems or prevention of dental disease in naval personnel.

APPROACH: Dental officers will conduct studies evaluating new techniques, materials, drugs, and equipment to compare them to those currently being used in Navy dentistry. These projects, carried out under the supervision of NNDC staff personnel will be continued as long as necessary to establish their value. Problems of immediate concern to dental practice in the U.S. Navy will be emphasized.

PROGRESS: A number of projects are currently being conducted to evaluate materials and/or techniques in endodontics, operative dentistry, periodontics, and prosthodontics. Some signigicant findings of the past year: (1) The bond strength of a bonding agent (Den-Mat) was found to be significantly greater than Adaptic (control) for repairing porcelain fractures of fixed partial dentures. (2) The chance of microleakage may actually be increased when the product of intermixing bases and varnishes is allowed to remain on the walls and margins of prepared teeth. (3) No relationship was found between the inflammatory response elicited by endodontic cements and the presence of a cell-mediated or delayed-type hypersensitivity. (4) Clinical impressions suggest that the primary value of the 'Swab Tip' may be in the maintenance of isolated periodontal defects, not in the control of generalized periodontal disease. (5) Surfaces of nonprecious metal should be treated with an abrasive air eraser and aluminum oxide powder to ensure a uniform surface with minimal contamination prior to porcelain application. (6) A nonprecious alloy can be recast for four generations with no alterations in tensile strength, Rockwell hardness, or percentage elongation. A total of 13 papers have either been published or accepted for publication. Several have been presented orally at scientific meetings.

SUPPORTED BY

U.S. Dept. of Defense, Navy, Naval Medical Research & Development Command, National Naval Medical Center	funds n.a.

13.0002, DEVELOPING A DENTAL RESOURCE MANAGEMENT SYSTEM

C.R. Jerge, University of Pennsylvania, Wharton School of Finance & Commerce, L Davis Inst of Health Economics, *34th & Spruce Sts., Philadelphia, Pennsylvania* 19104 (P50 HS 02577-030002)

This project is part of a broader program (HS 02577-03) whose summary states: The University of Pennsylvania National Health Care Management Center (NHCMC) is an interdisciplinary center for research, advanced education, and technical assistance in the area of health care management. This proposal is for continuation of the project into Year 03. The NHCMC brings together faculty from within the University of Pennsylvania and other institutions to work together on problems facing a variety of health delivery and health related institutions and organizations, with a primary focus on management.

As a result of a recently completed national needs assessment process, NHCMC will focus on leadership in programs related to institutional management; financial management; management of service delivery; environmental control and regulation; consumer behavior/education; and manpower and industry structure. Internally, NHCMC will pursue research projects related to reimbursement incentives and procedures, service delivery management and institutional management.

Other programs include a national doctoral research award program, numerous continuing education programs, and an active technical assistance and dissemination program, including a national newsletter, Interchange.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
Office of Health Research
Statistics & Technology,
National Center for Health
Services Research funds n.a.

13.0003, COMPETITION AS A MEANS TO CONTAIN DENTAL CARE COSTS

D.A. Conrad, University of Washington, School of Dentistry, Dept. of Community Dentistry, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195 (R03 HS 03603-01)

The purpose of this research is to examine various provisions of state dental practice acts and professional ethical codes, and then to determine their impact on the level and variation of the prices for dental services. Specifically, the study will be composed of three stages: 1. states will be categorized according to legal and ethical code restrictions on advertising, the employment and functions of dental auxiliaries, and the 'corporate' practice of dentistry; 2. the level and variation (among dentists) of prices for dental services will be measured for each state (and in certain cases for market areas within the state); and 3. a model will be developed which yields testable hypotheses with respect to the relationship between legal and ethical restrictions and the level and variation of prices for dental services.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
Office of Health Research
Statistics & Technology,
National Center for Health
Services Research $48,948

13.0004, ADAPTATION OF MEDICAL QUALITY ASSURANCE METHODS TO OUTPATIENT DENTAL CARE

H.L. Bailit, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *W. Spring St., West Haven, Connecticut* 06516 (689-001-I)

This two-year study addresses the need for practical, effective, and provider-acceptable quality assessment methods for hospital-based, outpatient general dental care. The goals are: 1) to adapt existing inpatient quality assessment procedures for use by outpatient dental services and 2) to develop protocols and instructions, compatible with JCAH and BQA policies, for use of these review methods by hospital dental programs.

The review procedures of interest are profile monitoring and Medical Care Evaluation Studies which include: 1) criteria list dental audits, 2) criteria mapping dental audits, and 3) health accounting. Three types of topics will be selected for the studies: common diseases or problems; discrete elements or procedures in the care process; and patient administrative process. A minimum of 25 topics will be used; for each topic explicit criteria will be developed, based on a literature review and consultation with experts.

A pretest of all criteria and methods will be completed to allow modification before actual use. Each review procedure will then be tested in five hospitals; the primary data source will be patient records and, to a lesser extent, patient questionnaires and examinations.

The revised protocol and assessment methods will be reviewed and used by 25 randomly selected dental programs; their comments will be incorporated into protocols which will be available to hospital dental programs nationally.

SUPPORTED BY

U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

13.0005, ADAPTATION OF MEDICAL QUALITY ASSURANCE METHODS TO OUTPATIENT DENTAL CARE

H.L. Bailit, University of Connecticut, Health Center, School of Dental Medicine, Dept. of Behavioral Sciences & Community Health, *Farmington Ave., Farmington, Connecticut* 06032

This two-year study addresses the need for practical, effective, and provider-acceptable quality assessment methods for hospital-based, outpatient general dental care. The goals are 1) to adapt existing inpatient quality assessment procedures for use by outpatient dental services and 2) to develop protocols and instructions, compatible with JCAH and BQA policies, for use of these review methods by hospital dental programs.

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The revised protocol and assessment methods will be reviewed and used by 25 randomly selected dental programs; their comments will be incorporated into protocols which will be available to hospital dental programs nationally.

SUPPORTED BY

American Fund for Dental Health	funds n.a.

13.0006, DEVELOPMENT OF ORAL HEALTH STATUS FOR QUALITY ASSURANCE

M. Marcus, University of California, Los Angeles Campus, School of Dentistry, Section of Preventive Dentistry & Public Health, *405 Hilgard Ave., Los Angeles, California* 90024

The project will empirically derive oral health status indexes for both adults and children from the judgments of general dentists experienced in quality assurance. These experts select from each pair of 'simulated patient' cases, the case which is in better oral health according to the judge's own professional criteria. By using pairs of cases, the underlying variables regarding each dentist's perception of oral health are assessed and a score for each case is generated.

For the adult index, eighteen parameters relevant to dental health have been collapsed from 167 variables abstracted from each case. This data plus the dentists' judgments are input into a 'Paired Preference Program' developed by Mickey and Britt. The study design employs multiple evaluation of the cases yielding efficient estimates of the preferred variables without increasing the data base to compensate for patient-to-patient or dentist-to-dentist variability. The dentists' equations thus derived will be compared and the differences resolved according to a quantitative format. A composite score for each case will be used to validate the final components of the index. The index will be further validated on live patients in the clinic and tested against the judgments of practicing dentists.

These oral health status measures will play an important role in quality assurance and assessment as an evaluation tool for use by dental health plans, private practices, and planning agencies, as well as for student appraisal.

SUPPORTED BY

American Fund for Dental Health	funds n.a.

13.0007, DEMONSTRATION AND EVALUATION OF A DENTAL QUALITY ASSURANCE MODEL IN A PREDOMINANTLY RURAL STATE - MONTANA

P. Milgrom, University of Washington, School of Dentistry, Dept. of Community Dentistry, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195

OBJECTIVE: This project is a joint effort of the Montana Dental Association and the The Department of Community Dentistry, University of Washington, to develop a systematic voluntary quality assurance model for a predominantly rural state.

METHOD: The objective will be accomplished by development of a clinical self-assessment system involving 150-200 general dentists in the state of Montana. Particular emphasis is placed on developing practical, usable methods to maximize participation. Different approaches to seeking volunteer practices will be tried and evaluated. Two review cycles are anticipated involving restorative and prosthetic dentistry.

SUPPORTED BY

American Fund for Dental Health	funds n.a.

13.0008, A COMPARISON OF TWO QUALITY REVIEW SYSTEMS, PATIENT PERCEPTIONS

OF QUALITY AND CONSUMER AND PROVIDER ATTITUDES TOWARD QUALITY

R.L. Lindahl, University of North Carolina, Chapel Hill Campus, School of Dentistry, Depts. of Dentistry/Pedodontics, *Chapel Hill, North Carolina* 27514

In response to the growing demand for quality assurance in the health professions, this project is designed to study peer review for the private practitioner in general dentistry. The objectives of this study are to compare two quality assessment methods in private dental offices; 1) a review of dental records, including radiographs, medical history, clinical examination, treatment plan and record, and 2) a posttreatment clinical review of restorative procedures.

Another aspect of the project will investigate consumer and provider attitudes toward quality and means of maintaining or improving it. This will be accomplished with the use of questionnaires and personal interviews.

A group of dentists interested in participating in this project has been found and plans are currently underway for implementing a pretested data collection system in each of their offices. Data will be collected before, during and after the experimental phase of the project to assay the effect that peer review will have on each office.

A patient questionnaire to be given in each participant's office during the baseline period prior to the experimental phase of the project has been pretested and finalized and is ready to use.

SUPPORTED BY
American Fund for Dental Health funds n.a.

13.0009, TO INTEGRATE DENTISTRY INTO MEDICAL-NURSING CURRICULUM AND PROVIDE DENTAL CARE IN FEDERAL DISTRICT HEALTH DELIVERY SYSTEM

Unknown, National University of Mexico, *Mexico City, D.F., Mexico*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY
W.K. Kellogg Foundation $50,000

13.0010, TO DEVELOP A VOLUNTARY DENTAL QUALITY ASSURANCE MODEL FOR RURAL PRACTITIONERS BASED UPON PEER REVIEW AND SELF-ASSESSMENT

Unknown, University of Washington, Graduate School, *Seattle, Washington* 98105

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY
W.K. Kellogg Foundation $90,375

13.0011, TO ADAPT MEDICAL QUALITY ASSURANCE METHODS TO OUTPATIENT DENTAL CARE

Unknown, University of Connecticut, Health Center, Graduate School, *Farmington Ave., Farmington, Connecticut* 06032

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY
W.K. Kellogg Foundation $71,895

13.0012, TOWARD A RATIONAL APPROACH TO THE PREVENTION OF DENTAL DISEASE AND THE DELIVERY OF DENTAL CARE ON A STATEWIDE BASIS

J.W. Bawden, Dental Foundation of North Carolina, *c/o UNC School of Dentistry, Chapel Hill, North Carolina* 27514

The study was an extensive epidemiologic survey of dental disease and treatment in the North Carolina population; a careful evaluation of dental manpower in the state and an estimate of their current treatment productivity; and, an investigation of the effect of a dental insurance program on utilization of dental care services by a blue collar population. The results have been studied with respect to a number of dimensions, but the primary focus has been on improved dental manpower needs, projections and planning.

The epidemiological study was a replica of one conducted 15 years previously. Comparison data showed that in the population 30 years of age and younger the caries prevalence has declined and the proportion of caries treated has increased. On the other hand, periodontal disease in the non-white population has increased markedly. The practice survey showed that relatively little periodontal treatment is being rendered. The availability of a dental insurance program had minimal effects on utilization of dental preventive and treatment services.

SUPPORTED BY
W.K. Kellogg Foundation funds n.a.

13.0013, THAMESMEAD DENTAL HEALTH PROJECT

Emslie, University of London, Guys Hospital Medical School, *London Bridge, London SE1 9RT, England, United Kingdom*

A study of treatment patterns provided to a community receiving regular dental care at a health center, specifically oriented towards prevention of dental disease.

SUPPORTED BY
Medical Research Council $157,014

XIV. DENTAL ECONOMICS

14.0001, EVALUATION OF NAVY ORAL HEALTH PROGRAMS

M.R. Wirthlin, U.S. Dept. of Defense, Navy, Naval Dental Research Inst., Clinical Investigation Dept., *Great Lakes, Illinois* 60088 (DN741310)

The prevalence of oral diseases caused by bacterial plaques on the teeth is virtually 100%. The objective of this study is to improve the management of manpower and fiscal resources needed to care for these diseases by assessing severity of diseases, incidence of new lesions, identification of personnel with high risk of dental emergencies, and demonstration of the cost-effectiveness of new preventive and treatment programs of plaque control.

Longitudinal and cross-sectional clinical data will be collected to evaluate the dental and oral health of naval personnel. Epidemiological, dental public health, statistical, and data processing methods will be employed to monitor the effectiveness and cost benefit of existing and proposed programs of the Navy preventive dentistry effort.

SUPPORTED BY

U.S. Dept. of Defense, Navy,
Naval Medical Research &
Development Command,
National Naval Medical Center funds n.a.

14.0002, NATIONAL SURVEY OF ADULT DENTAL HEALTH 1978

P.M. James, University of Birmingham, *P.O. Box 363, Birmingham, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council $78,507

14.0003, AN EVALUATION OF THE UTILIZATION AND COST EFFECTIVENESS OF DENTAL AUXILIARIES IN THE NATIONAL HEALTH SERVICE

G.B. Winter, University of London, Eastman Dental Hospital, *Gray's Inn Rd., London WC1 8LD, England, United Kingdom*

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

Medical Research Council $28,589

XV. DENTAL EDUCATION

DENTAL STUDENTS

15.0001, MYO-ORAL FACIAL PAIN - A CURRICULUM/RESEARCH PROGRAM FOR ORAL HEALTH CARE PROFESSIONALS

J.L. Hiatt, University of Maryland, Baltimore Professional Schools, School of Dentistry, Dept. of Physiology, *66 W. Baltimore St., Baltimore, Maryland* 21201

A curriculum will be devloped beginning in the preclinical years whereby anatomical and physiological principles being learned may be translated into clinical concepts of occlusion as these relate to the function and dysfunction of the stomatognathic system producing the Myo-Oral Facial Pain Syndrome. The program in the first clinical year will incorporate the interdisciplinary approach to recognition, diagnosis, research and management. Further efforts in diagnosis, research and management will be broadened in the students' fourth year as the curriculum is expanded to include inter-professional faculty from medicine and other allied health professions culminating in clinical research and management of patients possessing the Myo-Oral Facial Pain Syndrome. Th project staff will also develop a multifaceted program of continuing education for the practicing professional updating his knowledge in the diagnosis and management of Myo-Oral Facial Pain Syndrome.

GOALS: To develop and evaluate a curriculum and research program for students at the predoctoral, postdoctoral and continuing education level in the recognition, diagnosis and management of myo-oral facial pain syndrome. These goals will be accomplished via intra/interdisciplinary interprofessional teaching and demonstration research projects.

SUPPORTED BY

American Fund for Dental Health $34,455

15.0002, TEACHING THE ACQUISITION OF PSYCHOMOTOR SKILLS IN DENTISTRY

W.F. Vann, University of North Carolina, Chapel Hill Campus, School of Dentistry, Dept. of Pedodontics, *Chapel Hill, North Carolina* 27514

Acquisition of psychomotor skills is one of the most important educational tasks in dental education; yet there has been little systematic research in this area. This ivestigation compared a traditional method of teaching psychomotor skills with a new approach which applied a relatively new theory of learning called the heavily guided systems approach.

The investigation was conducted in a twenty week preclinical restorative dentistry laboratory. Eighty-eight freshman students were randomly assigned to an experimental (n equals 44) or control group (n equals 44); instructors (n equals 44) were randomly assigned to each group. The controls were taught using the traditional teaching method used at the UNC School of Dentistry at Chapel Hill; the experimental group was taught using a systems approach which relied on detailed checklists and intensive faculty feedback. Dependent variables measured were: quality of performance on laboratory examinations; time required to complete these exams; and time required to complete the course.

Preliminary results suggest that this experimental approach has excellent promise for psychomotor skill teaching and learning in dentistry. A future study will investigate these same questions in clinical as well as preclinical dental school courses.

SUPPORTED BY
American Fund for Dental Health $10,754

15.0003, ERGONOMIC EQUIPMENT FOR DENTAL TREATMENT

E. Comhaire, Rijksuniversiteit te Gent, School of Dentistry, *B9000 Ghent, Belgium*

Since 1960 a series of prototypes for dental treatment equipment was planned, built and tested, leading to a universal type for every kind of treatment, for every working position of the dentist and every treatment position of the patient. Other conditions fulfilled were: working with or without assistance and having always every item of the equipment in a constant relation to the practitioner. Many other details were studied: control-systems, wash-basin, suction, operating light, tray-systems, etc. In addition several systems in dental practice administration and dental teamwork were tested out in the didactic build-up of the preclinical and clinical education in the school. All these principles were applied in the construction and equipment of the new dental school, to be completely finished in 1982. To this immediate goal was added the information from the study that went to dental industry, to dental students and practitioners.

SUPPORTED BY
Rijksuniversiteit te Gent funds n.a.

DENTISTS/SPECIALITY TRAINING

15.0004, STUDY AND CORRELATION OF CRITERIA FOR GENERAL PRACTICE DENTAL RESIDENCY PROGRAMS

J.M. Laracuente, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, Dental Service, *4100 W. 3rd St., Dayton, Ohio* 45428 (552-002-I)

The purpose of this study is to compare the different General Practice Dental Residencies with the VA programs and if feasible, make recommendations to the Veterans Administration Dental Professional Development Program as well as the ADA and AGD Councils on Dental Education.

A questionnaire has been sent to all Directors of General Practice Dental Residency Programs in the United States.

The answers will be analyzed and then prepared for publication.

SUPPORTED BY
U.S. Veterans Admin., Dept. of Medicine & Surgery funds n.a.

DENTAL AUXILIARIES

15.0005, TO DEMONSTRATE PRIVATE PRACTICE UTILIZATION OF EXPANDED-FUNCTION DENTAL AUXILIARIES TO IMPROVE PRODUCTIVITY AND ACCESS TO CARE

Unknown, University of Kentucky, Graduate School, *Limestone & Euclid, Lexington, Kentucky* 40506

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY
W.K. Kellogg Foundation $205,815

15.0006, TO DEMONSTRATE VALUE OF EXPANDED-FUNCTION DENTAL AUXILIARIES IN PRIVATE PRACTICE IN IMPROVING PRODUCTIVITY AND ACCESS TO CARE

Unknown, University of Washington, Graduate School, Office of Research in Medical Education, *Seattle, Washington* 98105

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY
W.K. Kellogg Foundation $249,465

DENTISTS/CONTINUING EDUCATION

15.0007, DEVELOPMENT OF CLINICAL CASE SIMULATION IN DENTISTRY

G. Jones, University of Nebraska, Lincoln Campus, School of Dentistry, *Lincoln, Nebraska* 68508 (N01LM94710 (CONTRACT))

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY
U.S. Dept. of Health & Human Services, Public Health Service,

National Inst. of Health,
National Library of Medicine $86,516

PATIENT EDUCATION/MOTIVATION

15.0008, PREVENTIVE DENTISTRY MEASURES OF MILITARY SIGNIFICANCE

T.C. Lyon, U.S. Dept. of Defense, Army, Medical Research & Development Command, Preventive Dentistry Div., *Washington, District of Columbia* 20012 (DA0E6022)

To develop new and simplified methods of preventing oral diseases and maxillofacial injuries. To assess new methods of (1) improving the biologic management of militarily relevant oral conditions and (2) improving the cost-effectiveness factors of preventive dental therapy in the military.

Studies will be conducted on military installations which will evaluate (1) methods of prevention of militarily relevant abnormalities and maxillofacial injuries- (2) methods of improving preventive dentistry delivery systems- (3) methods of improving cost-benefit ratios concerning delivery of preventive dentistry as a consequence of military duty- and (4) investigate the various hazards involved in the Army Dental Health Delivery System.

SUPPORTED BY
U.S. Dept. of Defense, Army,
Medical Research &
Development Command, Inst.
of Dental Research funds n.a.

15.0009, A NURSING INTERVENTION TO INCREASE INDEPENDENCE IN GOOD DENTURE BRUSHING TECHNIQUES OF NURSING HOME RESIDENTS

K. Dorsey, U.S. Veterans Admin., Dept. of Medicine & Surgery, Medical Center, *Roseburg, Oregon* 97470 (653-001-I)

The research was developed to approach the problem of nursing home patients becoming increasingly dependent upon staff to do tasks which could comfortably be done by themselves. The study will utilize structured training and expectations regarding denture brushing self-care and will compare experimental and control groups on the basis of 1) with special training and reinforcement (Experimental) vs 2) usual denture brushing practices on the NHCU (Control). The Null Hypothesis: There will be one difference in the level of independence demonstrated by subjects in the two research groups. Groups will be compared by t-test and the level of significance sought is .05. An evaluation instrument to measure levels of independence will be used. The instrument, developed by Mrs. Dorsey, consists of 17 items based on ADA and Roseburg Dental Service instructions. The instrument was reviewed for content validity by numerous professional staff. Data will be collected in two phases: 1) Pre-reinforcement and 2) post-reinforcement. All subjects to be rated by trained raters/observers.

SUPPORTED BY
U.S. Veterans Admin., Dept. of
Medicine & Surgery funds n.a.

15.0010, DEVELOPMENT AND FIELD TESTING OF HEALTH EDUCATION PROGRAMS INTEGRATED IN SCHOOL CURRICULA

K.G. Konig, Katholieke Universiteit Nijmegen, Inst. of Preventive & Community Dentistry, *Philips Van Leydenlaan 256800, Nijmegen, Netherlands*

In the Netherlands there is an urgent need for school health education programs which are adapted to the Dutch situation. At present, general health education program are not being put into practice in kindergarten and primary schools. Some subjects, e.g. safety in traffic, nutrition and nutrition related to dental health are being taught incidentally.

In Nijmegan a multidisciplinary team has been initiated to develop and evaluate a health education curriculum in which aspects related to nutrition, dental health, safety in traffic, energy expenditure and other fields will be integrated in a uniform way by using a 'conceptual approach'.

The aim of this project is to develop awareness of processes influencing health, decision making directed to a healthy growth and development, and evaluation of the total curriculum.

An essential part of the project is to evaluate the long-term somatic effects of these programs.

SUPPORTED BY
Government of Netherlands $52,216

CLINICAL CANCER EDUCATION

15.0011, NETWORK DEMONSTRATION PROJECT IN HEAD AND NECK CANCER

S. Silverman, Northern California Cancer Program Inc., *770 Welch Rd., Suite 190, Palo Alto, California* 94304 (N01CN55180 (CONTRACT))

The contractor has completed his planning year and is ready to implement at least twice the number of patients called for in the RFP at no appreciable increase in cost over the original cost estimate. A Project Officer visit is being planned for the fall to maintain close technical surveillance.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Cancer Inst. funds n.a.

15.0012, CLINICAL CANCER EDUCATION PROGRAM

S. Silverman, University of California, San Francisco Campus, School of Dentistry, Dept. of Oral Medicine & Hospital Dentistry, *551 Parnassus Ave., San Francisco, California* 94122 (R25 CA 17914-05)

Oral cancer accounts for approximately 5% of all cancers in the United States and is keeping pace with the relative yearly increase in cancer incidence. The overall 5 year survival in these malignancies is less than 40%. Therefore, public and professional awareness of early recognition and adequate management are essential. The objective is to combine demonstration and education in diversified multidisciplinary program of oral cancer control for undergraduate, graduate and postgraduate dental students and dentists, as well as medical and paramedical personnel. This will be accomplished through education in the following: early cancer detection and recognition of recurrence; methods of caring for dental and paradental tissues, before, during and after therapy; rehabilitation through replacement of missing tissues by prostheses and psychosocial intervention.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$87,078

15.0013, CLINICAL CANCER EDUCATION PROGRAM (DENTAL)

M.G. Martinez, University of Alabama in Birmingham, School of Medicine, Dept. of Pathology, *1919 7th Ave. S., Birmingham, Alabama* 35233 (R25 CA 17934-05)

The main objective of this proposal is to develop and implement an educational program to provide a broad and advanced knowledge of oral cancer to undergraduate students of dentistry, to postgraduate and graduate students, to practicing dentists, to auxiliary health personnel and to the public so that the quality of health care can be improved with the final result of a lower mortality rate from oral cancer.

This could be accomplished through: (1) undergraduate programs for dental students, dental hygienists and dental assistants above and beyond those provided in the regular curriculum of dental schools on oral cancer; (2) special education programs for graduate and postgraduate students with new concepts in early diagnosis and management of oral malignancies; (3) continuing education courses for practicing dentists, physicians and auxiliary personnel to improve the clinical skills in the detection, prevention and rehabilitation of patients with oral cancer and to stress the increasing responsibility of the dental profession in the multidisciplinary approach to the management of patients with complications following therapy for cancer of the oral and paraoral regions; and (4) educational programs for the general public in an attempt to make them aware of the importance of early detection in curability of oral cancer, as well as in prevention of oral lesions.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$53,224

15.0014, CLINICAL CANCER EDUCATION PROGRAM

P.A. Pullon, Washington University, School of Dental Medicine, Dept. of Pathology, *4559 Scott Ave., St. Louis, Missouri* 63130 (R25 CA 17966-05)

Washington University School of Dental Medicine proposes a Clinical Cancer Education Program which will coordinate and improve the teaching about neoplasia at the undergraduate, postgraduate and continuing education levels. Fundamentally this program will be a continuation and expansion of a previous program. At the undergraduate dental student level the following changes are proposed: 1) To improve, revise, and enlarge the self-teaching program in pathology, 2) to continue the autopsy and Radiation Oncology Screening Program rotations, 3) to enlarge the Oral Oncology course for senior dental students from sixteen to eighteen hours, 4) to create an eighteen hour course on dental radiology and 5) to continue the senior biopsy requirement. At the postgraduate level we propose to: 1) Enlarge the Advanced Oral Pathology course from eighteen to thirty-six hours with a great majority of this time devoted to the recognition of oral lesions and 2) to encourage the attendance and participation of the postgraduate students in the Oral Oncology course. At the continuing dental education level we propose to offer an all-day symposium on head and neck cancer for the dental profession (all of the dental profession, not just dentists) and to make this program available to our undergraduates and postgraduates at no cost.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$29,359

15.0015, CLINICAL CANCER EDUCATION PROGRAM

J.F. Newsome, University of North Carolina, Chapel Hill Campus, School of Medicine, Dept. of Surgery, *Manning Dr., Chapel Hill, North Carolina* 27514 (R25 CA 17973-05)

With the aid of professional educators (Office of Medical Studies), a combined program in the Schools of Medicine and Dentistry is planned to offer new and expand existing educational opportunities in oncology to selected predoctoral (some premedical) and postdoctoral students of medicine and dentistry, undergraduate and graduate nursing students and public health nurses. These programs will be incorporated where feasible into ongoing educational programs for predoctoral and postdoctoral students, and practicing physicians and dentists.

Traditional clinical oncology teaching will be enhanced by a curriculum which emphasizes clinical-biologic aspects of cancer, including carcinogenesis, new methods of diagnosis and treatment, methods of investigation and the socioeconomic and psychological impact of the disease.

The overall goal is not only to improve existing teaching methods but to attract the good student to oncology.

Methods include the utilization of a Computerized Cancer Data Base, an existing Area Health Educational Centers program, and existing educationally structured tumor clinics. Clincal assistantships and associateships with clinical investigation, self-instructional techniques, videotapes and film strips and other aids are some of the methods to be employed.

Methods of evaluation will include current practices (i.e. numbers of participants, future activities, daily assessments of progress skills and productivity) and the use of clinicologic problems and other techniques designed by the Office of Medical Studies.

SUPPORTED BY	
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$231,803

15.0016, CLINICAL CANCER EDUCATION PROGRAM (DENTAL)

W.R. Sabes, University of Kentucky, School of Dentistry, Dept. of Oral Pathology, *Limestone & Euclid, Lexington, Kentucky* 40506 (R25 CA 17992-04)

The proposed program will build upon our core of basic teaching of head and neck oncology to bring a more comprehensive knowledge of head and neck cancer to the dental student, the dental hygiene student and to dental and auxiliary practitioners. The emphasis will be placed upon accomplishing these goals with the dental and auxiliary practitioners by means of the Outreach Program. The objectives are to prepare practitioners to: 1) incorporate head and neck examination procedures into their practice of dentistry, 2) arrive at a definitive diagnosis of cancer, 3) understand and intelligently discuss with the patient referral to an oncologist, 4) be prepared to provide needed dental care before and after cancer treatment and 5) recognize the importance of, and direct the patient to, rehabilitative measures available to the patient. The Outreach Program of taking self-instructional packages to the practitioner in his or her office on an appointment basis will be continued and expanded. To expand the oncology teaching of the dental students, the self-instructional materials will be incorporated into the development of an elective course in head and neck oncology. Further, self-instructional packages will be developed to teach the lay public (patients) about various aspects of head and neck cancer. Evaluation of the effectiveness of those efforts will continue to be used to revise programs or to develop new instructional packages. These efforts will be an integral part of the Ephraim McDowell Community Cancer Network, Inc.

SUPPORTED BY	
U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$29,566

15.0017, CLINICAL CANCER EDUCATION PROGRAM (DENTAL)

N.J. Burzynski, University of Louisville, School of Dentistry, Dept. of Oral Diagnosis & Oral Medicine, *129 E. Broadway, Louisville, Kentucky* 40202 (R25 CA 18006-05)

The Clinical Cancer Education Program concerns itself with the instruction of undergraduate, graduate and auxiliaries in the current concepts of prevention, detection, diagnosis, treatment and rehabilitation of oral-facial cancer. Emphasis is placed on multidisciplinary approach to cancer detection and care, with emphasis on head and neck cancer. Evaluation of various educational experiences in cancer related topics is applied to various facets of the program. Computer Assisted Self-Evaluation (CASE) programs, Symposia, and Continuing Education Courses on both the institutional and outreach levels are presented to the practitioners and auxiliaries. Clinical Cancer Assistantships are offered to interested and qualified individuals.

BIBLIOGRAPHIC REFERENCES: George, D.I., Burzynski, N.J., and Miller, R.L. Reactive Properties of Oral Lesions to the Specific Red Cell Adherence Test. Oral Surg. 47:51-57, 1979. Burzynski, N.J., Kupchella, C.E., Calhoon, T.C., and Reid, K.H. The CASE System for Cancer Education. J. of Dent. Education. April 1979, in press.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Cancer Inst. $62,871

15.0018, CLINICAL CANCER EDUCATION PROGRAM

J. Beumer, University of California, Los Angeles Campus, School of Dentistry, Dept. of Removable Prosthodontics, *405 Hilgard Ave., Los Angeles, California* 90024 (R25 CA 18724-04)

The broad purpose of this program is to increase the diagnostic and therapeutic skills of dental students, practicing dentists, and associated paraprofessionals with regard to patients who have head and neck tumors. The method of approach to this educational problem includes incorporation of the basic educational program at UCLA School of Dentistry concerning cancer; and importantly, an expansion of the undergraduate teaching program through rotating two week block assignments. Practicing dentists and paraprofessionals would be included in this expanded program. Additional methods of education for professionals include postgraduate education and screening clinics in the general community.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Cancer Inst. $101,474

15.0019, CLINICAL CANCER EDUCATION (DENTAL)

C.A. Waldron, Emory University, School of Dentistry, Dept. of Oral Pathology, *106 Forest Ave. N.E., Atlanta, Georgia* 30303 (R25 CA 19253-04)

This project seeks to: improve and expand an ongoing cancer education program at Emory University School of Dentistry at the undergraduate, postgraduate and continuing education levels; develop a position of Clinical Associate in Oral Cancer at the postresidency level; develop two Clinical Assistantships in Oral Cancer at the undergraduate level; expand cancer education for dentists in the community and state and region; continue and expand the diagnostic and consultative services of Emory University School of Dentistry at all levels of the program in an effort to improve oral cancer detection and management.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Cancer Inst. $40,261

15.0020, CLINICAL CANCER EDUCATION PROGRAM (DENTAL)

R.P. Elzay, Virginia Commonwealth University, School of Dentistry, Dept. of Oral Pathology, *901 W. Franklin St., Richmond, Virginia* 23284 (R25 CA 19294-04)

The purpose of the application is to obtain financial assistance to improve cancer education for dental students, dental hygiene students, postgraduate students, faculty and practitioners beyond the content of the existing cancer program in the Dental School curriculum. The goals of the program will be: 1. To continue to improve and extend cancer education for undergraduates, postgraduates, dental hygienists, practicing dentists and faculty. 2. To make our dentists and patients aware of the existing informational material available through our Health-Line (Dial-A-Tape) Program and promote the use of these resources. 3. To implement a continuing educational oral cancer detection activity within the State of Virginia. 4. To continue an ongoing objective, orderly analysis and evaluation of the Oral Cancer Curriculum within the School of Dentistry. 5. To assist in the maintenance of the established Oral Tumor Registry, Computerized Oral Tumor Recall Program, and Recall and Referral Clinic as educational instruments at the undergraduate, graduate and postgraduate levels.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Cancer Inst. $33,856

15.0021, CLINICAL CANCER EDUCATION GRANT

A.H. Kutscher, Columbia University, School of Dental & Oral Surgery, Dept. of Stomatology, *Broadway & W. 116th St., New York, New York* 10027 (R25 CA 19424-03)

This Clinical Cancer Education Continuation Grant Application is again submitted following progress performed under a 8-year Clinical Cancer Training Program (undergraduate) at this institution, funded by NCI until termination on June 30, 1976 and specifically following refunding in part as of 7/1/77. In the present 3 year (7/77-6/80) Clinical Cancer Education Grant, now in progress in its second year, the constructs of the previous grant are being continued and where possible expanded. These include: a) integration and rotation of a student population (undergraduate dental students, dental hygiene students, and dental assistants) through related oncologic disciplines; b) emphasis on diagnosis and treatment; c) cooperation with all pertinent medical center departments, clinics, operating rooms, laboratories, head and neck tumor conferences and follow-up clinics, etc.; d) clinical stomatology conferences; e) an expanded series of didactic lectures; f) participation of dental students in the ongoing major elective in oral surgery; g) extensive orientation to psychosocial aspects of oral cancer and its management.

The current grant (operating for the second year) stresses again, among others, the following major new foci: 1) training regarding all facets of premalignant oral disease (including the concept of malignant transformation, care approaches employed in a clinic to be devoted to premalignant lesions, and familiarization with a nearly inaugurated premalignancy tumor registry for erosive and ulcerative lichen planus); 2) expanded (multiple approach) mouth care programs for all cancer patients; 3) major expansion of the multidisciplinary medical psychosocial program; 4) development of additional cancer-oriented, new diagnostic and care (pain) research programs.

BIBLIOGRAPHIC REFERENCES: Zegaralli, D.J. and Zegarelli, E.V. Chrondroma of the Tongue - Case Report with Ultrastructure and a Review of Literature. Oral Surgery, 43:738-745, 1977.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$19,437

15.0022, CLINICAL CANCER - DENTAL

A.S. Miller, Temple University, School of Dentistry, Dept. of Pathology, *3223 N. Broad St., Philadelphia, Pennsylvania* 19122 (R25 CA 19456-04)

Temple University School of Dentistry proposes institution of a Clinical Cancer Education Program to coordinate, expand and augment cancer education at the undergraduate and postgraduate levels, as well as the dental hygiene and continuing education programs. Part of the program will be conducted at extramural locations, such as Temple University Hospital and American Oncologic Hospital, by the coordinator of hospital dentistry. This will provide hospital and tumor clinic exposure for dental students and dental hygiene students. We propose continuing a program of oral health care for patients undergoing radiation therapy for malignant oral, head and neck neoplasms, involving graduate students in periodontology and dental hygiene students. The general program objectives are to: (1) provide undergraduate and postgraduate dental students and dental hygiene students with the basic principles of cancer biology, epidemiology, detection, diagnosis, treatment, prevention and control; (2) establish appropriate attitudes and motivation for continued learning about cancer, which will carry over into the practice years; and (3) develop and foster concepts of cooperative humane care for the oral cancer patient, especially oral rehabilitative care. The overall administration of the Clinical Cancer Education program will be through the Department of Pathology in cooperation with the Cancer Education Committee and the Departments of Oral Surgery and Oral Diagnosis.

BIBLIOGRAPHIC REFERENCES: Miller, A.S., Leifer, C., Chen, S.-Y. and Harwick, R.D.: Oral granular cell tumors. Oral Surg., 44:227-237, 1977. Chen, S.-Y. and Harwick, R.D.: Ultrastructure of oral squamous cell carcinoma. Oral Surg., 44:744-753, 1977.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$36,748

15.0023, CLINICAL CANCER EDUCATION PROGRAM - DENTAL

G.W. Greene, State University of New York, Health Science Center at Buffalo, School of Dentistry, Dept. of Oral Pathology, *3435 Main St., Buffalo, New York* 14214 (R25 CA 19504-02)

The proposed cancer education program intends to coordinate our presently comprehensive core curriculum with several special programs designed to broaden the scope of our present curriculum. It plans to review all present aspects of cancer education taught in oral pathology, oral medicine, oral surgery, and prosthetics and the affiliated hospital dental programs. These programs will be integrated into a structured form which will benefit dental assistants, dental hygienists, dental students, medical students and postdoctoral trainees and practicing dentists. This present program will be augmented by a cancer education program specifically for faculty members in all areas of the school. The development of a program on cancer awareness, in cooperation with the local and regional dental society members, will be instituted. A hospital program for postdoctoral trainees, specifically related to head and neck cancer, will be implemented. Development of various videotapes to demonstrate these activities for future use and demonstration will also be implemented. To establish a monthly meeting for faculty and interested practitioners will be an additional goal; during such meetings interesting head and neck cancer patients will be seen in one of the departments or hospital services. Indoctrination and expansion of duties for dental hygienists and assistants will be part of the faculty education program.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Cancer Inst. $47,714

15.0024, CLINICAL CANCER EDUCATION PROGRAM (DENTAL)

G.A. McCarty, University of Tennessee, Center for the Health Sciences, School of Dentistry, Dept. of Oral Diagnosis, *62 S. Dunlap St., Memphis, Tennessee* 38103 (R25 CA 19532-04)

OBJECTIVES: To develop and maintain an active, coordinated approach to clinical cancer education for the dental community. To increase competence of the students in the oral cancer screening examination, biopsy, and cytology techniques and to promote their routine use in general practice. To provide increased clinical experience in the dental management and treatment of oral cancer. To provide the opportunity for the student to become proficient in the dental management of patients receiving radiotherapy and chemotherapy treatment for head-and-neck cancer. To provide increased opportunity for students to participate in maxillofacial prosthetic rehabilitation procedures for head-and-neck cancer patients. To provide continuing cancer education of both a clinical and a didactic nature for the dental practitioners of this geographical area.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Cancer Inst. $51,321

15.0025, CLINICAL CANCER EDUCATION (DENTAL)

J.B. Lepley, Memorial Hospital for Cancer & Allied Diseases, *1275 York Ave., New York, New York* 10021 (R25 CA 20681-03)

The objective of this program is to educate three Clinical Associates annually in an A.D.A. approved curriculum in maxillofacial prosthetics.

The Associates will receive both clinical and didactic training in all aspects of maxillofacial prosthetics, particularly those aspects relating to the treatment of patients with head and neck cancer. The education they receive at Memorial Hospital will be multidisciplinary and will include clinical involvement with such areas as radiotherapy, chemotherapy, surgery, rehabilitation, etc.

The Associates will also attend lectures and courses at the New York University College of Dentistry and the U.S. Naval Graduate School of Dentistry. These lectures and courses, combined with lectures and seminars to be attended at Memorial Hospital, will provide strong academic training in both maxillofacial prosthetics and cancer treatment.

The Associates will receive education and training that will enable them, upon graduation, to assume faculty and staff positions at dental schools, medical centers, and cancer centers. These individuals, when assuming such positions, will have the broad viewpoint of cancer patient management so vital to the multidisciplinary approach necessary for both teaching and clinical practice.

SUPPORTED BY

U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Cancer Inst. $84,040

15.0026, CLINICAL CANCER EDUCATION PROGRAM

E.F. Cataldo, Tufts University, Boston Campus, School of Dental Medicine, Dept. of Oral Pathology, *136 Harrison Ave., Boston, Massachusetts* 02111 (R25 CA 20849-02)

An integrated preclinical and clinical cancer education program for all undergraduate dental students is proposed utilizing combined resources of Tufts University School of Dental Medicine, Tufts University School of Medicine and the New England Medical Center Hospitals. The objectives of the program are directed to preparing the dental student to: Better understand and appreciate the nature of cancer problems and principles of their management in order to enable them to practice better dentistry; develop improved skills in the diagnosis and management of oral cancer; develop the ability to recognize or suspect certain cancer problems which may come to their attention and appreciate the need for and technique of referring patients with such problems to physician colleagues.

The overall educational program may be summarized as: 1. Preclinical dental science of oral oncology: a. Introduction to oral oncology. b. Oral pathology of cancer. c. Oral oncology lectures. 2. Introduction to clinical medicine: a. Physical diagnosis: History and physical exam. b. Medical lectures: General pathology, oral pathology, oral medicine, head and neck cancer, laboratory medicine, clinical pharmacology. 3. Clinical medicine: a. Medical lectures (ear, nose and throat, common malignancies, chemotherapy, radiotherapy). b. Hospital clerkship (medical oncology, radiotherapy, otolaryngology).

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$65,295

15.0027, CLINICAL CANCER EDUCATION PROGRAM

R.O. Greer, University of Colorado, Medical Center, School of Dentistry, Dept. of Oral Biology, *4200 E. 9th Ave., Denver, Colorado* 80220 (R25 CA 21098-03)

The objectives of the clinical cancer education curriculum at the University of Colorado School of Dentistry are threefold. The first objective is to enhance the diagnostic acumen of our dental students, practicing dentists, faculty and associated health professionals as it relates to the detection of neoplasia of the head and neck. A second goal is to increase the management and therapeutic competence of all the above-mentioned in the realm of head and neck neoplasia. The third objective is to reinforce the concept of a team approach to the prevention, diagnosis and treatment of head and neck neoplasia.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$42,223

15.0028, CLINICAL CANCER EDUCATION GRANT

R.S. Verbin, University of Pittsburgh, School of Dental Medicine, Dept. of Pathology, *C336 Salk Hall, Pittsburgh, Pennsylvania* 15213 (R25 CA 22547-02)

It is the objective of this program to augment our basic cancer education curriculum with an integrated, readily identifiable, multidisciplinary didactic course coupled with expanded clinical experiences. The didactic component will be structured into a new block of curricular time which will represent a required course for the entire third year class of dental students. Additional clinical experiences will be provided via participation in the various activities of the Regional Center for Maxillofacial Prosthetic Rehabilitation. In this latter facility, the students will be engaged in: (1) The further development of skills in proper examination procedures; (2) teaching patients a routine that can be utilized for self-examination of the oral cavity; (3) pretherapeutic evaluation of new cancer patients; (4) management of irradiated patients; (5) management of patients on chemotherapeutic regimens; (6) operating room procedures; (7) providing dental care for oral cancer.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Cancer Inst.	$29,599

15.0029, CLINICAL CANCER EDUCATION PROGRAM - ORAL ONCOLOGY

H.M. Goldman, Boston University, School of Dentistry, Dept. of Oral Pathology, *755 Commonwealth Ave., Boston, Massachusetts* 02215 (R25 CA 22980-02)

The Clinical Cancer Education Program at the School of Graduate Dentistry has developed a series of activities to meet the stated objectives set forth in the grant. It was noted that the general philosophy was to provide dental students and practitioners with sufficient training and education in oncology. The program is aimed at the undergraduate and graduate dental students who participate in didactic lecture courses and case demonstrations. Further impact is evident through the presence and training of a Clinical Associate in oral oncology who interacts with the Departments of Otolaryngology, Medical Oncology, Radiation Oncology, Surgical Oncology, Maxillofacial Prosthetics, and Oral Medicine.

Six students have volunteered to participate in the one-month oral oncology elective. Also an educational program in oncology, dental education, and the dental care of patients receiving radiation or chemotherapy has been planned with the Division of Continuing Education of the School of Graduate Dentistry.

A separate Department of Oral Oncology has been established with the Program Director of this grant application (the Co-P.I.) designated as the Professor and Chairman. An Oncology Committee has been organized comprising the chairpersons of each of the Departments as well as physicians in the Departments of Nutrition, Otolaryngology, Radiation Therapy, Surgical Oncology and Medical Oncology.

A faculty of medical, surgical, radiation, and head and neck oncologists, as well as specialists in nuclear medicine, rehabilitation, radiology and pathology, has been integrated into the oncology program of the School of Dentistry.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Cancer Inst. $56,590

15.0030, ORAL AND HEAD AND NECK CLINICAL CANCER EDUCATION PROGRAM

F.S. Watkins, University of Oklahoma, Health Science Center, School of Dentistry, Dept. of Continuing Dental Education, *Box 26901, Oklahoma City, Oklahoma* 73190 (R25 CA 24677-01A1)

This project will design and implement additions to a multi-disciplinary education program which addresses three major components of dental care in oral and head and neck cancer. These are: 1) specific preventive measures, 2) health promotion, and 3) knowledge and ability to provide prompt diagnosis, treatment and follow-up. The program consists of educational activities for dental health professionals and consumers. The education activities for dental health professionals will provide sources of training, coordination and an information exchange for Oklahoma dental students, dental hygiene students and dental practitioners. The consumer education program will provide information on oral cancer and instruction in self-examination for persons identified as regular dental patients and for the public sector which may or may not seek regular dental care.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Cancer Inst. $48,795

15.0031, CLINICAL CANCER EDUCATION PROGRAM

G. Shklar, Harvard University, Boston Campus, School of Dentistry, Dept. of Oral Medicine & Oral Pathology, *188 Longwood Ave., Boston, Massachusetts* 02115 (R25 CA 26182-01)

A comprehensive and multidisciplinary program of education in clinical oral cancer aimed at improving the early diagnosis, treatment and overall care of the patient with oral cancer, as well as the oral care of all cancer patients, particularly those undergoing active therapy. The program will involve undergraduate dental students; graduate dental students; dentists, physicians, dental hygienists, dental assistants, visiting nurses, public health nurses and other health personnel in the community; medical students, interns and residents in the various Harvard affiliated hospitals. Subject matter will deal with all phases of the oral cancer treatment ranging from prevention, through screening, diagnosis, therapy, up to rehabilitation. The teaching of oral and dental care for all cancer patients will be developed and presented to undergraduate and graduate dental students as well as to dentists and auxiliary dental personnel in the community, with clinical experience in the setting of a Comprehensive Cancer Center as well as in other appropriate facilities. A major part of the program will be the continued development of graduate education in oral oncology, with three clinical associates per year receiving training and experince in all phases of oral cancer management, providing an opportunity for developing comprehensive skills in a specialized field of oral oncolgy such as maxillofacial prosthetics.

SUPPORTED BY
U.S. Dept. of Health & Human
Services, Public Health Service,
National Inst. of Health,
National Cancer Inst. $66,576

XVI. DENTAL MANPOWER

DENTISTS

16.0001, DETERMINANTS OF PRACTICE PATTERNS AMONG WOMEN IN DENTISTRY

J.K. Wittemann, Virginia Commonwealth University, School of Dentistry, Dept. of Community Dentistry, *901 W. Franklin St., Richmond, Virginia* 23284

Although recent literature has presented discussions on the perceptions of women in dentistry held by the public and male practitioners, and there is a concern that the public does not get its full value from the woman dentist, no systematic investigation of practice patterns among women in dentistry has been reported. The overall purpose of this project is to conduct a study of the determinants of practice patterns among women in dentistry in order to establish baseline data that will permit the profession to better understand the role of women in the profession and to project this knowledge to practice trends.

The groups to be studied include female practitioners and two comparative groups of male practitioners: psycho-social factors which effected their selection of dentistry as a career; formal education factors which effected the development of their career plans; factors related to the student-practitioner transition that are anticipated to effect practice plans; psycho-social factors influencing their selection of dentistry as a career; characteristic of practice, such as practice locale, practice style, specialty practice, professional relationships, workload and extra-professional endeavors; factors that have influenced practice patterns, such as family responsiblility or life style preferences, level of community and/or colleague acceptance and career changes. The data obtained will be coded by cohort and a form of discriminant analysis will be employed in the analysis.

The proposal project is to be accomplished in four phases over two years. Phase one will focus on refinement of the theoretical frame-work to be employed in the construction of the two survey instruments and development of the survey instruments. Phase two and phase three involve the survey procedures for the three groups and phase four involves the between, and within group analysis resulting in the final report.

SUPPORTED BY

American Fund for Dental Health	$13,236

DENTAL AUXILIARIES

16.0002, NAVY DENTAL TECHNICIAN UTILIZATION

D.M. Anderson, U.S. Dept. of Defense, Navy, Naval Dental Research Inst., Clinical Investigation Dept., *Great Lakes, Illinois* 60088 (DN877418)

TECHNICAL OBJECTIVE: Surveys of civilian dental practices indicate dentists' incomes increase with use of ancillary personnel and extra dental operating rooms (DOR). Further economies are expected in group practices. The aim of this effort is to evaluate the effectiveness of Navy dental officers utilizing Navy dental technicians in conventional and new DOR settings and modes of practice.

APPROACH: In order to assess optimum utilization of dental manpower, the effectiveness of dental care delivery will be determined for a group of Navy dental officers who will operate with one or more auxiliaries and one or more DOR's in conventional, separate DOR and new, radial DOR settings. Factors of personal preference which influence dentists' utilization of dental auxiliaries will also be evaluated. The formulation of training programs and use of additionally trained auxiliaries for dental specialties will follow.

PROGRESS: First and second year dental officers and dental technicians were observed to be more productive as a team than when dental officers worked with occasional assistance. Restorative procedures were comparable in conventional and new DOR settings, but more periodontic and oral hygiene procedures were done in the new DOR. The test group of first and second year dental officers provided more operative dentistry treatment procedures when each used two dental operatories instead of one. Percent effectiveness also increased with greater technician utilization. The use of a rotating dental assistant in addition to the chairside assistants was not cost-effective. Identification of task areas in endodontics which can be assumed by specially trained assistants has been completed and materials and methods for their inservice training are in preparation. One (1) technical report.

SUPPORTED BY

U.S. Dept. of Defense, Navy, Naval Medical Research & Development Command, National Naval Medical Center	funds n.a.

16.0003, THE UTILIZATION OF EXPANDED FUNCTION AUXILIARIES IN PRIVATE PRACTICE IN WASHINGTON STATE

P. Milgrom, University of Washington, School of Dentistry, Dept. of Community Dentistry, *D-322 Health Sciences, SC-62, Seattle, Washington* 98195

The project is being conducted jointly by the Washington State Dental Association and the Center for Health Services Research, University of Washington. The project is one part of the national program of the W.K. Kellogg Foundation to evaluate the impact of the use of expanded function dental auxiliaries in the private practice of dentistry in the United States.

One hundred thirty-five dental practices and approximately 500 dental personnel are participating in this evaluation project. These practices were chosen to be representative of general dental practices in the State.

OBJECTIVES OF THE PROJECT: The goal of the evaluation is to examine the effect of increased use of expanded function dental auxiliary personnel on the viability of dental practices. Four major questions are being addressed: 1. Is the productivity of a private practice increased through the utilization of expanded duty dental auxiliaries (EDDAs)? 2. What changes in the dental practice result from the utilization of expanded function dental auxiliaries? 3. How does the utilization of expanded duties impact on practice members? 4. How does the utilization of expanded duty dental auxiliaries affect patients' attitudes and the care they receive?

DEMONSTRATION PROGRAM: The demonstration program consists of continuing dental education, practice-specific feedback, and consultation in dental practice management. The program will be available to all staff members of the participant practices.

EVALUATION DESIGN: Participant practices are recruited to the project for a two-year period. At the beginning of the first year, the practices are randomly assigned to experimental and control groups. The experimental group will participate in the demonstration program during the first year while the control group receives no special attention. During the second year the first-year control group becomes the second-year experimental group; it will participate in the demonstration program while the original experimental group becomes the second year control group.

SUPPORTED BY

W.K. Kellogg Foundation	funds n.a.

16.0004, EFFECTS OF EXPANDED FUNCTION DENTAL AUXILIARIES (EFDA'S) IN DENTAL PRACTICE IN KENTUCKY - A STATEWIDE DENTAL DEMONSTRATION PROJECT

R. Mullins, University of Kentucky, School of Dentistry, Dept. of Community Dentistry, *Limestone & Euclid, Lexington, Kentucky* 40506 (UHTSO7A)

On December 1, 1977, the University of Kentucky began work on a four-year demonstration project funded by the W.K. Kellogg Foundation to demonstrate the effects which increased use of expanded function auxiliaries (EFDA's) and practice management systems will have on private dental practices in Kentucky. The demonstration will examine effects in the areas of production, income, expenses, patient satisfaction, management, provider satisfaction, and quality. In addition, factors that may influence the use of EFDA's will be examined. The project is divided into six phases: Phase I: December 1977 -October 1978; Project Planning and Design; Phase II: November 1978 - April 1979; Baseline Data Collection; Phase III: April 1979 - June 1979; Management Training; Phase IV: July 1979 - March 1980; Auxiliary and Dentist Training in Expanded Functions; Phase V: April 1980 -September 1980; Steady-State Data Collection; Phase VI: October 1980 November 1981; Preparation of Reports. Production and expense data are being collected continuously in Phases II - V. Fifteen private dental offices are participating in this project.

SUPPORTED BY

W.K. Kellogg Foundation	$250,000

XVII. MISCELLANEOUS

17.0001, COMMITTEE ON RESEARCH AND MANPOWER OF THE NATIONAL ADVISORY DENTAL RESEARCH COUNCIL

R.E. Bradley, U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research, National Advisory Dental Research Council, *9000 Rockville Pike, Bethesda, Maryland* 20205 (R09 DE 03936-03S6)

No summary has been provided to the Smithsonian Science Information Exchange.

SUPPORTED BY

U.S. Dept. of Health & Human Services, Public Health Service, National Inst. of Health, National Inst. of Dental Research	$24,900

INVESTIGATOR INDEX

Aaronian, A.J. -2.0232
Abbey, L.M. -3.0018
Abdelmoumene, M. -10.0037
Ackerman, J.L. -4.0054
Acton, E.M. -1.0193
Acuna, N.R. -4.0061*
Adamiak, J. -9.0104
Adderly, D.D. -1.0129, 1.0260
Adey, J.D. -9.0006
Adrian, J.C. -3.0001*, 11.0014*
Aduss, H. -5.0006*, 5.0007*, 5.0045. 6.0010, 7.0015*, 7.0016*
Agatstein, N. -1.0311
Agudelo, U. -3.0073
Aguirra, -1.0158
Akveld, F.N. -1.0023
Albert, D.M. -3.0011*
Albino, J.E. -7.0034*
Aleff, H.J. -10.0080*
Aleski, C. -1.0124
Alexander, J. -1.0310*
Alfano, M.C. -2.0052, 2.0084*, 3.0030*, 5.0016
Alicea, M. -10.0073
Allen, B.M. -10.0030
Allen, G.D. -7.0032
Allen, G.E. -5.0044, 7.0031
Allen, L.H. -2.0207*
Alling, C. -9.0053
Alling, C.C. -15.0013
Allison, J.D. -11.0023*
Allmann, D.W. -2.0248*
Altman, L.C. -2.0087*
Amato, P.R. -10.0052, 10.0071
Amdur, B.H. -2.0049*
Amsbaugh, S.M. -1.0159, 1.0166, 1.0194, 1.0261
Anbar, M. -1.0231*
Anderson, D.J. -10.0044*
Anderson, D.L. -1.0032, 3.0082*
Anderson, D.M. -3.0160, 9.0074, 16.0002*
Anderson, H.C. -4.0044*
Anderson, K.V. -3.0029
Anderson, M. -3.0090
Andres, R. -5.0033
Anusavice, K.J. -9.0058
Appelbaum, B. -2.0015, 2.0257
Aramany, M.A. -15.0028
Arceneaux, J.E. -1.0122
Archard, H.O. -3.0037
Argen, P. -11.0035
Argentar, H. -9.0021
Ariet, M. -7.0055
Armitage, G. -2.0286
Armstrong, J.A. -3.0008*
Arndt, W.B. -5.0050
Arnesen, S. -1.0048, 2.0077, 4.0097
Arnold, R.R. -1.0149*, 1.0197
Arvidsson, J. -10.0030
Asaro, J.P. -2.0105
Asgar, K. -9.0061*
Ash, G. -7.0053
Ash, M.M. -7.0053*
Ashrafi, S. -3.0081
Aten, J. -6.0014*
Attebery, H.R. -2.0029
Atwood, D. -15.0031
Austin, M. -3.0122
Austin, W.L. -4.0030, 5.0038
Avery, J.K. -4.0067*
Ayres, A. -1.0114, 1.0115
Azen, E.A. -3.0107, 3.0134*
Azzam, N. -5.0041
Baboolal, R. -2.0236*
Bacon, C. -1.0046, 2.0076
Badellino, F. -3.0060*
Bader, J. -16.0004
Badger, S.J. -2.0018*
Baehni, P.C. -2.0088, 2.0108
Baer, J.E. -1.0289
Baer, M.J. -4.0054, 7.0006
Baer, T. -4.0092
Bahn, A.N. -11.0003, 11.0037
Bahn, S.L. -11.0003*, 11.0025*, 13.0004
Baier, R.E. -9.0081
Bailey, W.F. -9.0027*
Bailey, W.J. -9.0011
Bailit, H.L. -1.0314*, 10.0087*, 13.0004*, 13.0005*
Baker, J.R. -2.0073*
Baker, T.R. -10.0081
Bakker, V.M. -8.0001*
Balian, G. -2.0067
Banes, A.J. -2.0161
Banks, E. -1.0298
Banoczy, J. -1.0195*, 3.0074*
Banting, D.W. -1.0006, 1.0007*
Bardach, J. -5.0047
Baret, J. -6.0009
Barnett, M.L. -1.0123, 2.0061*
Baron, R. -2.0210
Barrach, H. -2.0176, 3.0085, 4.0020, 7.0005
Barrett, W. -1.0046, 2.0076
Barsumian, E. -2.0124
Bartner, H. -4.0045
Basciano, L. -2.0124
Bassett, C.A. -2.0229*
Bassham, D.R. -15.0024
Bataini, P.G. -3.0064
Bateman, B. -2.0182
Battistone, G.C. -2.0184*, 11.0006
Baum, B.J. -1.0232, 3.0112*, 3.0140, 4.0072
Baumgarten, R.F. -15.0019
Baumrind, S. -4.0076*, 7.0038*
Bawden, J.W. -1.0276*, 4.0063*, 13.0012*
Bayley, D. -10.0041
Baylink, D.J. -2.0194*
Bays, R.A. -7.0046*
Beaman, A.J. -1.0099
Bear, S.E. -15.0020
Bearman, J.E. -3.0092
Beaudoin, A.G. -2.0074
Beck, C.M. -7.0048*
Beck, J. -1.0202
Beer, M. -2.0080
Beery, Q. -7.0051
Behling, U. -2.0097
Behling, U.H. -2.0045
Beigelis, A.A. -9.0043
Bekhor, I. -4.0007*, 5.0013*
Belcourt, A.B. -1.0048, 2.0077, 4.0097
Bell, W.H. -7.0044*
Bell Berti, F. -4.0092
Bender, I.B. -3.0158
Benedetti, C. -10.0053
Bennett, C.G. -7.0055
Bennett, G.J. -10.0037*
Benveniste, K.B. -2.0171*, 2.0172*
Ben Zvi, A. -2.0131
Berg, S.L. -2.0051
Bergner, M. -16.0003
Berkovitz, B.K. -2.0082*
Berkowitz, R.J. -1.0015*
Bernstein, D.A. -10.0062
Berry, H.H. -11.0018*
Bessette, R.W. -2.0247. 15.0023
Beumer, J. -15.0018*
Beutner, E.H. -1.0002*, 2.0105
Bey, R.F. -2.0039
Bhooshan, B. -5.0021*
Bhown, M.B. -2.0162
Bick, P. -2.0103
Biedenbach, M.A. -10.0042*
Billings, R.J. -1.0032
Bird, W.C. -2.0282*, 3.0158*, 9.0119*
Birdsell, D.C. -2.0036*, 2.0113
Bishop, B. -7.0057
Bissell, G.D. -1.0326*
Bixler, D. -5.0002*, 5.0033*
Blakley, G.A. -4.0029
Blankenship, J.R. -2.0252*, 7.0027*
Bleiweis, A.S. -1.0004*, 1.0134*
Bloch, P. -11.0035
Block, S.L. -10.0077
Bloom, C. -2.0278, 2.0279
Bluestone, C.D. -5.0046
Blum, H. -4.0078
Boass, A. -2.0195, 2.0199
Bodden, R.W. -15.0013
Bolender, D.L. -4.0013
Bolle, N. -7.0039
Bonaterra, L.M. -4.0056*
Bond, W.H. -3.0100
Bonica, J.J. -10.0001*, 10.0053
Bonnaud, A. -2.0149, 4.0050
Bonner, J.J. -5.0035, 5.0039
Bookstein, F.L. -4.0039
Boone, M.E. -15.0027
Borden, B. -9.0118
Borgstein, J.I. -3.0045
Bornstein, P. -2.0067*
Boshell, J.L. -3.0147*
Boskey, A.L. -1.0177*
Bosma, J.A. -3.0112

*INDICATES PRINCIPAL INVESTIGATOR

INVESTIGATOR INDEX

Bosma, J.F. -4.0045*, 4.0054*, 4.0071*, 5.0052*
Boucher, L.J. -11.0015
Bouquot, J.E. -2.0141
Bourke, G.J. -3.0067
Bourret, L.A. -4.0094
Bowden, G. -3.0112
Bowden, G.H. -1.0012
Bowen, R.L. -9.0021*, 9.0023
Bowen, W.H. -1.0009, 1.0084, 1.0085, 1.0102, 1.0129, 1.0132, 1.0133, 1.0155, 1.0156, 1.0158, 1.0159, 1.0160, 1.0166, 1.0194*, 1.0216, 1.0217, 1.0218, 1.0233, 1.0260, 1.0261, 1.0282, 1.0302*, 1.0304, 1.0305*, 3.0112
Bowley, W.W. -7.0010, 7.0020
Boyan Salyers, B.D. -2.0255*, 4.0096*
Boyd, D.D. -1.0293*
Boyle, M. -7.0010
Bozzola, J.J. -1.0300*
Bracke, J.L. -1.0032
Bradbury, D.R. -1.0209
Braden, M. -9.0052*
Bradley, B.E. -4.0067
Bradley, R.E. -17.0001*
Bradley, R.M. -4.0010, 4.0073*
Brady, J.M. -9.0114*
Brady, L.W. -3.0087*
Bragg, S. -1.0011
Brand, J.G. -10.0041*
Brantley, W.A. -9.0063*
Brascho, D.J. -15.0013
Breakstone, R. -1.0311
Breinig, M.C. -3.0008
Breitling, S.M. -9.0104
Brennan, P.C. -1.0125
Brenner, C.M. -1.0229
Breytenbach, H.S. -3.0044
Brinkley, B. -2.0169
Brinkley, L.L. -5.0011*
Broadwell, R.D. -3.0121
Brown, D.A. -2.0036
Brown, D.G. -3.0146*
Brown, D.M. -15.0024
Brown, E. -10.0030
Brown, F.J. -10.0031*
Brown, J. -2.0228, 4.0022
Brown, K.S. -1.0284, 2.0182, 4.0030*, 5.0038*
Brown, L.R. -1.0105*, 1.0211*, 2.0242
Brown, S.D. -9.0110*
Brown, T. -12.0005*
Brown, V.J. -1.0232, 4.0072
Brown, W.E. -1.0041*, 1.0067*, 1.0070*, 1.0214, 9.0023*
Brownell, A.G. -4.0004*
Brudevold, F. -1.0043*
Brugere, J. -3.0064*
Brunelle, J. -1.0158
Brunelle, J.A. -1.0201*, 1.0215, 1.0277, 1.0278, 1.0281, 1.0282
Brunetti, A.P. -1.0041
Brunner, D.G. -15.0008
Brunski, J.B. -9.0087*
Brunson, D. -9.0116
Budner, S. -1.0311
Budnick, S.D. -15.0019
Bugg, C.E. -1.0062*
Bulkacz, J. -2.0037*
Bullock, R.A. -11.0016
Bullock, W.W. -2.0143*
Bullough, P.G. -1.0177
Burdi, A.R. -4.0040*, 7.0002*
Burkitt, D.P. -3.0045
Burn Murdoch, R.A. -7.0018*
Burnstein, E. -10.0074
Burstone, C.J. -7.0020*, 7.0039*
Burt, B.A. -1.0119*
Burton, J.L. -3.0029
Burzynski, N.J. -15.0017*
Bussell, N. -2.0184
Bussell, N.E. -11.0011
Butler, D.P. -7.0042, 7.0049, 10.0071
Butler, S. -10.0053
Butler, W.T. -2.0162*, 4.0065*
Butts, H.C. -15.0024
Byers, B.R. -1.0122*
Byers, M.R. -10.0019*
Bytell, D.E. -3.0096, 9.0056
Caffesse, R. -2.0264
Caffesse, R.G. -2.0155*
Cagan, R.H. -10.0043*
Cagle, J.R. -1.0026, 1.0036
Calhoun, N.R. -1.0165*, 2.0233*
Calingaert, A. -2.0291
Cambron, R.E. -9.0060
Campbell, S. -9.0092
Canfield, R.C. -10.0009
Cantin, E.M. -3.0005
Caplan, A. -1.0101, 2.0078
Caplan, A.I. -1.0091*, 2.0066*, 2.0206*
Caplow, M. -2.0246*
Caputo, A.A. -9.0069
Caputo, C.B. -1.0101, 2.0078
Carchman, R.A. -2.0090*
Carl, W. -15.0023
Carlson, D. -4.0041
Carlson, D.S. -7.0047*
Carnes, D.L. -2.0220*
Carr, C.W. -1.0268*
Carroll, G.W. -2.0029*
Carson, K.A. -2.0072, 3.0130
Carter, C. -2.0125
Carter, S.K. -3.0094*
Casciani, F.S. -1.0052*
Caslavska, V.B. -1.0256
Cassel, J.M. -9.0041*
Castleberry, D.J. -15.0013
Catalanotto, F.A. -1.0290*
Cataldo, E.F. -15.0026*
Caterson, B. -2.0073
Cave, C.O. -3.0040
Cecil, J.C. -11.0001*
Cederquist, K.R. -7.0012
Celesk, R. -1.0175, 2.0024
Cervenka, J. -6.0007
Cesar, E.Y. -1.0025
Cha, C. -3.0006
Chace, N.M. -1.0175, 2.0024
Chacko, C.M. -5.0001
Chambers, D.A. -2.0286*
Chan, M. -2.0279
Chan, W.B. -10.0078
Chandran, K.B. -9.0084
Chang, A. -1.0114, 1.0115
Chang, Y. -1.0112*
Chapko, M.K. -16.0003
Chapman, C.R. -10.0053*
Charles, A.K. -1.0112
Charon, N.W. -2.0041*
Chase, W. -7.0039
Chasen, W.H. -2.0281
Chassy, B.M. -1.0128*
Chatrian, G.E. -10.0002*, 10.0009*
Chatterjee, R. -1.0144
Chaudhry, A. -15.0023
Chaudhry, A.P. -3.0088
Chaudhry, I.M. -3.0081
Chauncey, H.H. -2.0002*, 2.0226
Chen, L.Y. -10.0054*
Chen, P.B. -2.0121*
Chen, R. -10.0056
Chibuzo, G.A. -4.0047
Chiego, D.J. -4.0067
Chierici, G. -7.0009
Chierici, G.J. -7.0013*
Chilton, N.W. -1.0020
Chiu, T. -1.0117*, 1.0124*
Choih, S. -1.0127*
Chow, L.C. -1.0041, 1.0067, 1.0070, 1.0214
Christensen, C.M. -10.0026*
Christner, P.J. -2.0069*
Chung, S.I. -2.0240*
Ciardi, J.E. -1.0102*, 1.0160*, 1.0217, 1.0305
Ciarlone, A.E. -10.0027*
Ciola, B. -13.0004
Cisar, J.O. -2.0028, 2.0046, 2.0051*
Clagett, J. -2.0094*
Clagett, J.A. -2.0142*, 2.0166
Clark, B.A. -10.0071
Clark, G.E. -3.0160*
Clark, G.T. -10.0028*
Clark, R.E. -7.0040
Clark, R.L. -5.0025
Clark, R.W. -10.0029*
Clark, W.B. -2.0050*
Clarkson, B.H. -1.0150, 1.0254*
Cleveland, R.F. -1.0174
Clewell, D.B. -1.0208*
Click, E.M. -2.0067
Coburn, R.A. -3.0118*
Coccaro, P.J. -4.0075, 4.0080
Cochran, M.A. -9.0016
Coffey, J.C. -4.0085*
Cogan, M.I. -3.0143*
Cohen, B. -1.0308*, 2.0137*
Cohen, D.W. -11.0036*
Cohen, E.N. -11.0002*
Cohen, G.H. -3.0004*
Cohen, M.M. -6.0008*
Cohn, D.V. -2.0214*
Cohn, Z. -2.0129
Cole, M.F. -1.0155*, 1.0156, 1.0157*, 1.0158*, 1.0159*, 1.0194, 1.0303*, 1.0305, 3.0112
Coleman, P.H. -3.0018
Coleman, R.A. -2.0291
Coley, E.R. -1.0178
Colman, G. -1.0292*
Comhaire, E. -15.0003*
Conn, K.M. -1.0048, 2.0077, 4.0097
Conrad, D.A. -13.0003*
Converse, J.M. -4.0028*, 4.0075*, 4.0079*, 4.0080*
Cook, P. -3.0045
Cook, S.D. -9.0083
Cooke, F.W. -9.0108*
Cooper, F.S. -4.0092
Cooper, H.L. -2.0239
Cooper, S.A. -10.0070*
Corah, N.L. -10.0065*, 10.0086
Corcoran, B.A. -2.0289
Coriell, S. -3.0139
Coron, M. -2.0275
Corpron, R.E. -4.0067
Costanzo, G.A. -1.0167
Cotton, W.R. -3.0161*
Courtney, R.J. -3.0018
Cousins, R.J. -2.0250*
Cowart, B. -4.0070
Cowart, B.J. -1.0232, 4.0072
Cowin, S.C. -9.0084
Cowman, R.A. -1.0147*, 1.0161, 1.0162*
Cowsar, D.R. -1.0241*, 1.0260, 9.0046*, 9.0071*
Cox, C.F. -4.0067
Coykendall, A.L. -2.0005*
Craig, R.G. -1.0030, 9.0014*, 9.0048
Cramer, H.J. -1.0188, 2.0270
Cramwinckel, B. -15.0010
Cranley, R. -2.0182

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*INDICATES PRINCIPAL INVESTIGATOR

INVESTIGATOR INDEX

Cranley, R.E. -4.0030, 5.0038
Creamer, H.R. -2.0262*
Crenshaw, M.A. -1.0274*, 1.0276, 2.0198*
Crigger, M. -2.0062
Crosby, G. -1.0192*
Crowle, A.J. -2.0022*
Cuello, J.J. -3.0061*, 9.0034*, 9.0035*, 9.0123*
Culberson, J.L. -10.0011
Cullen, B.L. -3.0035
Cuprak, L.J. -3.0059*, 11.0004*
Curley, M.D. -8.0005
Curtiss, R. -1.0108*
Curzon, J. -1.0014
Curzon, M.E. -1.0038*, 1.0061*
Cutler, L.S. -2.0207
Cutright, D.E. -8.0003, 9.0101*
Cypek, J. -11.0003
Dabbous, M.K. -2.0169*
Daftary, D.K. -3.0065, 3.0066, 3.0104
Dagle, G.E. -9.0080
Dale, B. -2.0243*
Dale, B.A. -3.0055*
Daley, T. -2.0171
Dalgard, D. -1.0260
Dalgard, D.W. -1.0176*
Daneo Moore, L. -1.0110, 1.0174*
Daniels, C.A. -3.0009*
Daniels, T. -15.0012
Daniels, T.E. -3.0035
Darling, A.J. -2.0083*
Das, S. -9.0083
Dave, R.I. -3.0047
Davenport, R.E. -2.0276*
David, H.A. -3.0140
David, O.J. -4.0057*
Davidovitch, Z. -6.0012, 7.0003*
Davidson, S. -10.0075
Davis, M.E. -1.0162
Dayer, J.M. -2.0131
Dayoub, M. -11.0033
Debski, B. -2.0090
deCaceres, C. -4.0061
deCaceres, C.G. -3.0156*
Decker, J.L. -3.0006
DeGraff, B.A. -1.0047, 1.0048, 1.0049, 1.0051, 1.0052, 2.0077, 2.0182, 2.0228, 3.0139, 4.0022, 4.0097
deGutierrez, O. -4.0061
Dejter, S.W. -1.0048, 2.0077, 4.0097
DeLarco, J.E. -2.0134
Deleo, J. -1.0046, 2.0076
Delfino, J. -15.0014
De Luca, L. -4.0030, 5.0038
De Luca, S.M. -1.0101, 2.0078
Denny, P.C. -3.0108*
DePaola, D.P. -5.0016*
Depaola, P.F. -1.0316*
Derkson, G.D. -1.0167*
Desnick, R.J. -6.0007
Devore, D. -2.0171
DeVore, D.P. -9.0038*
Dewhirst, F. -2.0201
Diamond, L.S. -2.0026
Diaz, E.A. -7.0004*
Dichter, M. -9.0037*
Dijkman, D.J. -5.0009*
Dinius, A. -15.0020
Dinowitz, M. -2.0060*
Dionne, R.A. -10.0050, 10.0052, 10.0071*
DiRienzo, S. -1.0148
Dirks, O.B. -1.0023*
Dirksen, T.R. -2.0037
Dobbing, J. -4.0059*
Dobersen, M.J. -3.0122
Dodson, C.A. -11.0018
Dogon, I.L. -1.0328*
Doherty, N. -1.0200*
Doine, A.I. -3.0121
Dolby, A. -3.0034*
Domoto, P. -10.0067
Dong, W.K. -10.0003*
Donkersloot, J.A. -1.0100*
Dooner, J. -9.0033
Dooner, J.J. -2.0234*, 2.0235*, 2.0253, 2.0256
Dorf, D.S. -5.0042, 7.0030
Dorfman, H. -2.0282, 9.0119
Dorman, F.D. -7.0021
Dorsey, K. -15.0009*
Dorst, J.P. -6.0006
Dostrovsky, J.O. -10.0025*
Dougherty, S.F. -2.0125
Dowd, F.J. -3.0083*
Dowden, W.E. -9.0116
Doyle, R.J. -1.0212*
Drach, J.C. -3.0013*
Dreizen, S. -1.0211
Dreyer, D. -10.0007
Dreyer, D.A. -4.0068*
Dreyer, W.P. -3.0044
Driscoll, E.J. -10.0071
Driscoll, W.S. -1.0259*, 1.0277, 1.0278*, 1.0279, 1.0281
Drummond, J.F. -2.0052*, 15.0016
Dubner, R. -10.0032*, 10.0034, 10.0037, 10.0049, 10.0050, 10.0051, 10.0052, 10.0058
Duckworth, J. -1.0187, 2.0269
Duckworth, R. -1.0012, 1.0225*
Dudley, K.H. -4.0034, 5.0010
Dugan, S.A. -11.0031*
Duke, P.C. -3.0029
Durant, J.R. -15.0013
Dworkin, S.F. -10.0061*
Dwyer, A.J. -1.0188, 2.0270
Dyck, P.J. -10.0084*
Dziak, R.M. -2.0221*
Dziewiatkowski, D.D. -2.0074*
Eames, W.B. -9.0008
Eanes, E.D. -1.0049*
Eastoe, J.E. -1.0136*
Eberhart, R.C. -7.0044
Eberlein, D. -1.0084, 1.0304
Ebersole, J. -2.0101
Ebersole, J.L. -1.0297, 2.0106
Edgar, W.M. -1.0133, 1.0156*, 1.0166*, 1.0194, 1.0261*
Edidin, M.A. -5.0034*
Edwards, J.L. -2.0138
Eick, J.D. -9.0018
Einhorn, L.H. -3.0100
Einspahr, R.M. -1.0062
Eisenberg, R.J. -3.0004
Eisenmann, D.R. -1.0028*
Elashoff, R. -7.0038
ElAttar, T.M. -2.0258*
Ellen, R. -1.0007
Ellen, R.P. -1.0006*
Ellis, C. -1.0232, 4.0072
Ellis, C.D. -13.0004
Ellison, S.A. -1.0076*, 1.0152*, 1.0153, 3.0155
ElMofty, S. -15.0014
ElMofty, S.K. -2.0223*
Elzay, R.P. -15.0020*
Elzinga, M. -1.0046, 2.0076
Embery, G. -1.0088*
Emilson, C. -1.0084, 1.0133*, 1.0160, 1.0194, 1.0217*, 1.0218*, 1.0305
Emilson, C.G. -1.0260
Emmings, F.G. -1.0296
Emslie, -13.0013*
Eng, A.M. -4.0087
Engel, L.D. -2.0094, 2.0142
England, M.C. -2.0282, 9.0119
Engle, J.H. -9.0005
Enlow, D.H. -4.0053*
Ennever, J. -2.0242
Enwonwu, C. -2.0151*
Epstein, J.B. -3.0027*
Erb, R.A. -9.0045*
Erdman, A.G. -7.0021
Eschen, S. -9.0111
Espinal, -1.0158
Espinosa de Restrepo, H. -3.0073*
Etzel, K.T. -2.0250
Eubig, C. -11.0023
Evans, C.A. -4.0042*
Evans, H.E. -4.0047*
Evans, R. -1.0231
Evans, R.T. -1.0296*, 3.0118
Evans, S.G. -3.0046, 3.0103
Evaskus, D.S. -10.0077
Fairhurst, C.W. -9.0015, 9.0017, 9.0058*
Falls, W. -10.0030
Falls, W.M. -10.0035*
Fan, P.L. -1.0030, 1.0186
Farber, P.A. -3.0020
Farbman, A.I. -5.0001*
Farrar, J.J. -2.0128*, 2.0132
Farrar, W. -2.0128
Farrar, W.F. -2.0134
Farris, C.L. -1.0230
Fauquet, M. -4.0008
Fazio, M. -3.0060
Fehrman, S. -10.0083
Feingold, R. -9.0079
Fejerskov, O.E. -3.0092
Feldman, M.I. -15.0029
Feldman, R.S. -2.0226*, 2.0230*
Feldmann, R. -1.0046, 2.0076
Feller, R.P. -2.0062, 3.0141*, 9.0095, 11.0015*
Ferguson, A. -1.0090*
Fewell, T. -1.0187, 2.0269
Fields, H.L. -10.0023*
Fietzek, P. -1.0101, 2.0078
Fillery, E.D. -1.0006
Fine, A.S. -2.0241*
Fineberg, E. -3.0019
Finegold, S.M. -2.0031
Finerman, G.A. -2.0203
Fink, M.L. -2.0239
Fiori, T. -2.0287
Fischer, T.E. -9.0049*
Fischer, W. -15.0028
Fischman, S. -3.0113
Fischman, S.L. -3.0039*, 3.0040, 3.0118
Fisher, H.B. -3.0096
Fishman, S.R. -1.0321*
Fitzgerald, D.B. -1.0118*, 1.0161
Fitzgerald, J.E. -2.0036
Fitzgerald, R.J. -1.0118, 1.0147, 1.0161*
Fitzgerald, T. -2.0039
Fleiss, J.L. -1.0020*
Fleming, S. -2.0196, 9.0077
Fleming, W.W. -1.0050, 2.0079
Fletcher, G.H. -3.0078*
Fletcher, R.D. -9.0104*
Floyd, S.W. -1.0048, 1.0049, 1.0052, 2.0077, 2.0182, 2.0228, 3.0139, 4.0022, 4.0097
Flynn, G.L. -3.0014*
Flynn, H.E. -9.0081
Foidart, J. -2.0176, 3.0085, 4.0020, 7.0005
Folio, J. -2.0026, 7.0042
Folk, J.E. -2.0239*
Fonseca, M. -3.0156
Fonseca, M.M. -3.0127*, 3.0128
Fonseca, R.J. -4.0095*

*INDICATES PRINCIPAL INVESTIGATOR

INVESTIGATOR INDEX

Fontaine, J. -4.0008
Ford, J. -2.0073
Ford, S.J. -9.0005
Forney, J.A. -1.0178
Forrest, E.J. -4.0051*, 4.0086*, 5.0046*, 5.0048*, 5.0049*
Forrest, W.R. -3.0161
Foshager, V.D. -2.0276
Fowler, B.O. -1.0047*
Fowler, C. -4.0092
Fox, J.L. -1.0025, 1.0069*, 1.0248, 3.0014
Fox, P. -2.0133
Fox, P.C. -2.0127, 2.0130*
Francohenao, A. -3.0073
Franquin, J.C. -1.0170*, 1.0190*
Franzblau, C. -3.0133
Frechette, A.R. -9.0089
Freedberg, I.M. -3.0012*
Freedman, H. -9.0079
Freedman, M.L. -1.0171
Freedman, R. -10.0075
Freer, R.J. -1.0180*, 2.0090
Freidline, C.W. -9.0095*, 11.0015
Freund, T.S. -1.0199*
Friday, G. -7.0051
Friedman, L.A. -1.0242*, 1.0245*, 1.0324*
Friedman, P.P. -1.0178
Friedman, R.D. -3.0107*, 3.0110*, 3.0134
Friedman Kien, A.E. -3.0015
Fritz, M.E. -3.0132*
Froum, S. -2.0275, 9.0091
Fuentes, E.I. -11.0030*
Fuerstenau, D.W. -1.0066*
Fuesting, M.L. -11.0037*
Fuhr, A. -13.0004
Fujimoto, J. -7.0055
Fuller Bonar, J. -2.0128
Furr, M. -5.0050
Furstman, L.L. -10.0012*
Gabriel, O. -1.0080*, 2.0028, 2.0051
Gadol, N. -3.0035
Gage, A. -15.0023
Gage, A.A. -2.0247
Gage, J.P. -4.0032*
Gaik, G.C. -4.0037*
Gaines, J.F. -9.0074
Gale, E.N. -10.0065, 10.0086*
Galich, J.W. -1.0239, 3.0160
Galil, K.A. -11.0032*
Gallis, B. -2.0067
Gallo, O.J. -2.0288
Ganfield, M. -1.0173
Gangal, S.G. -3.0072*
Gangarosa, L.P. -3.0019
Gans, C. -7.0024*
Garant, P.R. -2.0107*
Garbarino, J. -1.0170
Garcia, D.A. -2.0272, 2.0281, 4.0099*, 9.0094*
Garman, T.A. -9.0017
Garn, S.M. -4.0040, 7.0002
Garrett, S.E. -11.0017
Gasser, D.L. -5.0028*
Gaugler, R.W. -1.0204
Gauthier, J.J. -1.0149
Gay, C.V. -2.0202, 2.0208
Gay, S. -2.0163
Gay, T. -7.0056*
Gay, T.J. -4.0092
Gebhardt, B.M. -2.0113*
Gebhart, G.F. -10.0039
Geddes, D.A. -1.0087*, 2.0047*
Geedes, D.A. -2.0035*
Gehrig, J.D. -10.0053
Geister, D.E. -7.0053
Gelman, R.A. -2.0080*
Genco, R. -1.0231
Genco, R.J. -1.0296, 2.0013*, 2.0102*, 2.0140*, 2.0266*, 3.0017*, 3.0118
Gendelman, H. -2.0288*, 3.0127, 3.0128*
Gentry, G.A. -3.0016*
Geoffrey, V. -4.0071, 5.0052
Gerencser, M.A. -2.0028
Germaine, G.R. -1.0127
Gershen, J. -13.0006
Gerson, S.J. -3.0081
Gessain, R. -3.0092
Gettleman, L. -9.0020
Gherna, R.L. -1.0003*
Ghia, J. -10.0008
Ghoneim, S. -3.0146
Giansanti, J.S. -15.0016
Gibbons, R. -2.0012
Gibbons, R.J. -1.0077*, 2.0048*
Gibbs, C.H. -7.0023*, 7.0055*, 7.0058
Gibson, F.M. -1.0131
Gill, S.P. -3.0143
Gillespie, G. -1.0158, 1.0263
Gillespie, G.W. -1.0001*
Gillette, W.B. -2.0274, 9.0092*, 9.0093*
Gilliam, L. -2.0283
Gilman, R.S. -2.0156*
Gilmour, M.N. -1.0014*
Gilpin, R.W. -1.0300
Ginsberg Felner, F. -3.0122
Glackin, R.N. -6.0006
Gladner, J.A. -2.0240
Glaros, A.G. -10.0075*
Glassman, A.H. -1.0162
Glimcher, M.J. -2.0189*
Glomski, C.A. -11.0021
Gmelig Meyling, F. -2.0125
Go, P. -1.0035
Gobel, S. -10.0030*, 10.0035, 10.0036, 10.0038
Goebel, N.K. -2.0249
Gold, H.O. -6.0011*
Goldberg, J. -7.0039
Goldberg, L.J. -4.0089*
Goldhaber, P. -2.0193*, 2.0226
Goldman, A.S. -5.0027*, 6.0003*
Goldman, H.M. -15.0029*
Goldstine, S.N. -3.0106
Golitz, L.E. -15.0027
Golub, E.E. -2.0070
Golub, L.M. -2.0168*
Gomez, I.M. -1.0194, 1.0302, 1.0305
Gomez, L.O. -4.0057
Gomez de Ferraris, M.E. -4.0057
Gong, J.K. -11.0021*
Gonyea, W.J. -7.0044
Goode, R.L. -3.0151*
Goodman Bicker, H. -1.0148
Goodson, J.M. -2.0053*, 2.0201*, 2.0286
Goodson, M. -2.0265
Goodwin, D. -3.0151
Gordon, N.C. -10.0023
Gorlin, R.J. -6.0007*
Gorman, J.J. -2.0239
Gorniak, G.C. -7.0024
Gould, H.J. -5.0042, 7.0030
Gould, R.G. -11.0024*
Gowgiel, J.M. -3.0054
Graber, L.W. -7.0041, 10.0074*
Graber, T.M. -7.0012*, 7.0041*
Grabowski, G. -6.0007
Gracely, R.H. -7.0042, 10.0033, 10.0049, 10.0050*, 10.0051, 10.0052*
Graham, M.M. -15.0001
Graham, S. -3.0039, 3.0040*, 3.0113*
Grant, A.A. -9.0099*
Grant, R.C. -9.0088
Gratt, B. -11.0024
Graves, M. -2.0135
Graykowski, E. -3.0140
Graykowski, E.A. -3.0037*
Green, D.B. -2.0144*
Green, K. -3.0019
Green, P.A. -1.0015, 1.0215
Greenberg, A. -7.0036
Greenberg, H.A. -7.0042
Greenberg, J. -3.0139
Greenberg, J.H. -4.0024*
Greenberg, R. -10.0052
Greene, C.S. -10.0077
Greene, G.W. -15.0023*
Greene, R.M. -3.0121
Greener, E.H. -9.0010*
Greenspan, D. -3.0035
Greenspan, J.S. -3.0025*, 3.0035*
Greer, R.O. -15.0027*
Gregg, J.M. -2.0072, 3.0130, 10.0007*, 10.0008*, 10.0085*
Gregory, T.M. -1.0070
Grobler, S.R. -1.0089
Gromer, J.I. -9.0092
Gron, P. -1.0256*
Gronas, D.G. -9.0042*
Gross, A. -2.0260*, 11.0033*
Gross, B.D. -7.0056
Grossman, N.S. -1.0209
Grower, M.F. -11.0006*
Guerra, O. -15.0014
Guertler, H. -3.0092
Gulmen, S. -15.0014
Gumprecht, J. -2.0203
Gunderson, J.S. -1.0313*
Gupta, O.P. -2.0065*
Gupta, P.C. -3.0065, 3.0066, 3.0104
Guralnick, W. -15.0031
Guralnick, W.C. -10.0078
Guttman, J. -3.0161
Gwinnett, A.J. -9.0022*
Haber, J. -1.0301*
Hackney, J.F. -5.0030*
Haffajee, A. -2.0265
Hagerty, R.F. -5.0051*
Hailer, A. -1.0049, 1.0051
Hall, C.W. -9.0107*
Hall, D. -7.0046
Hall, D.J. -5.0044, 7.0031, 7.0032
Hallsworth, A.S. -1.0074*, 1.0191
Halstead, C.L. -15.0019
Hamilton, J.W. -2.0214
Hamlet, S.L. -5.0043*
Hammond, B.F. -1.0107*
Hammouda, O. -2.0169
Hamner, J.E. -3.0066, 3.0104
Han, S. -1.0069
Hancock, E.B. -14.0001
Hand, A.R. -3.0121*, 3.0139
Handelman, S.L. -1.0229*, 9.0040
Handley, S.P. -1.0135*
Hanker, J.S. -1.0182*, 2.0071*, 2.0072*, 3.0129*, 3.0130*, 3.0136*, 10.0085
Hanks, C.T. -9.0048
Hansel, V. -2.0218
Hansen, C.T. -2.0129
Hardie, J.M. -1.0012
Hardwick, -1.0264*
Hargreaves, A. -15.0031
Harkins, S.W. -10.0053
Harp, R.J. -3.0019
Harper, D.S. -1.0079
Harrell, W. -1.0011
Harris, F.A. -9.0105*
Harris, J.E. -7.0006*, 7.0014*
Harris, K.S. -4.0092*
Harris, R.R. -3.0084*
Harris, S.S. -1.0164, 2.0059

*INDICATES PRINCIPAL INVESTIGATOR

INVESTIGATOR INDEX

Hart, T.R. -1.0121, 1.0154
Hartmann, F. -10.0046
Hartwick, G. -9.0088
Harvey, R.J. -9.0081
Harvold, E.P. -4.0091, 7.0009*, 7.0037*
Hascall, G.K. -2.0182*
Hascall, V.C. -1.0101*, 2.0078*
Hasse, A.L. -9.0089
Hassell, J. -1.0101, 2.0078
Hassell, T.M. -2.0173*
Hassler, C. -11.0012
Hassler, C.R. -9.0072*
Hasty, D.L. -4.0019*
Hata, R. -2.0215
Hattingh, J. -3.0125*
Hauge, G. -10.0068
Haughey, B. -3.0040
Haughey, B.P. -3.0113
Hausmann, E. -2.0104*
Hawley, C.E. -2.0123*, 11.0010*
Hawley, P. -3.0057
Hawley, R.J. -1.0130, 2.0284
Hay, D.I. -1.0143*, 1.0151
Hayduk, S. -2.0171
Hayes, M.L. -1.0220*
Hayes, R.L. -10.0058*
Hebert, N. -1.0233
Heeley, J.D. -4.0036*
Heft, M.W. -10.0049, 10.0050, 10.0051
Hegger, W. -15.0010
Heifetz, S.B. -1.0234, 1.0258*, 1.0277*, 1.0278, 1.0279, 1.0283*
Helman, J.C. -2.0183
Helsel, W. -2.0126
Hench, L.L. -9.0088*
Herity, B.A. -3.0067*
Hernandez, M. -3.0006
Herp, A.V. -3.0053*
Hertert, R. -11.0007
Hewitt, A.T. -2.0178, 4.0023, 5.0031
Hiatt, J.L. -15.0001*
Hiatt, W.H. -2.0232
Hicks, M.J. -1.0235*
Higgins, M.L. -1.0110
Higuchi, W.I. -1.0025*, 1.0069, 1.0248*, 3.0014
Hilfiker, M. -2.0128
Hilfiker, M.L. -2.0134
Hill, H.H. -9.0060
Hill, J.M. -3.0019*
Hill, M.W. -3.0028
Hillman, J.D. -1.0096*
Hillman, R.E. -9.0038
Hirano, H. -2.0203
Hirsch, P.F. -2.0173, 2.0197*
Hirschman, R. -10.0066*
Ho, B. -3.0121
Ho, M. -3.0008
Ho, N.F. -3.0014
Hock, J.M. -2.0092*
Hockfield, S.J. -10.0038*
Hoerman, K.C. -2.0064*, 3.0054*
Hoffeld, J.T. -2.0133*
Hoffert, M.J. -10.0037, 10.0052
Hoffman, D. -10.0034*
Hoffman, S. -15.0013
Hohl, T. -7.0054
Hohl, T.H. -4.0081*
Holcomb, D.W. -1.0026, 1.0036
Holdeman, L.V. -2.0014, 2.0020
Holden, S. -7.0053
Holliday, M.J. -6.0006
Hollins, M. -4.0068
Holmes, R.E. -9.0097*, 9.0098*
Holmstrup, P. -3.0062*, 3.0075
Holt, S.C. -2.0021*, 2.0023
Hook, W.A. -2.0124, 2.0130
Hooks, J.J. -3.0006*, 3.0037
Hopkins, K.P. -1.0146
Hopps, R.M. -2.0138, 3.0033, 3.0046, 3.0103
Horigan, E.A. -4.0021, 4.0024, 5.0019
Hornbuckle, G.C. -10.0059*
Horowitz, A.M. -1.0259
Horowitz, H.S. -1.0258, 1.0277, 1.0279*, 1.0281, 1.0283
Horton, J.E. -1.0178
House, J.E. -2.0281*, 11.0019*
Howard, G. -2.0194
Howes, R.I. -9.0120*
Hruska, K.A. -2.0223
Hsieh, H.S. -1.0164, 1.0291*
Hsu, H.H. -4.0044
Hsu, S.C. -1.0117
Hsu, S.D. -1.0155, 1.0157, 1.0158, 1.0303
Hu, J.W. -10.0015
Hubbard, V.S. -3.0140
Hudson, J.T. -9.0032
Huettner, C. -1.0111
Huffner, W. -15.0027
Huget, E.F. -9.0001*, 9.0055*, 10.0083*, 11.0007*, 11.0008*, 11.0034*
Hughes, C.V. -2.0276
Huis in't Veld, J.H. -1.0023
Hull, D.S. -3.0019
Hull, E. -1.0128
Hull, E.M. -1.0100
Hummeler, K. -6.0003
Hunt, C.E. -2.0200*
Hurel, C. -1.0237*
Hussain, M.Z. -2.0175*
Hutchens, L.H. -2.0173
Hutt, M.S. -3.0045*
Hyde, R.J. -3.0141
Hylander, W.L. -7.0011*
Iacono, V.J. -1.0148, 2.0107
Iker, H. -1.0014
Iker, H.P. -1.0229
Illing, S.J. -10.0065
Inal, E.C. -3.0070*
Iorio, R.J. -5.0029*
Ivanyi, L. -2.0063*
Iversen, J.M. -1.0141, 2.0056
Ivey, J. -2.0194
Izutsu, K. -3.0144*
Jackson, E. -10.0063*, 10.0069*
Jackson, R. -2.0164
Jacobson, A.P. -7.0055
Jacobson, B.J. -5.0026*
Jacques, N. -1.0115
Jacques, N.A. -1.0114
Jafek, B.W. -15.0027
James, P.M. -1.0168*, 14.0002*
James, R.A. -9.0095
Janoff, D. -2.0164
Jansons, D. -2.0272
Jayant, K. -3.0041*
Jee, W.S. -2.0225
Jelinski, L.W. -1.0050, 2.0079
Jendresen, M.D. -9.0018
Jenny, J. -1.0202*
Jensen, J. -3.0089
Jensen, O.E. -9.0040*
Jenson, A.B. -3.0057*, 3.0122
Jerge, C.R. -13.0002*
Jilka, R.L. -2.0214
Jochen, D.G. -9.0069*
Johnson, A.F. -5.0050
Johnson, A.H. -3.0115*
Johnson, D. -1.0285
Johnson, D.A. -3.0152*
Johnson, D.C. -10.0011*
Johnson, F.B. -15.0027
Johnson, H. -10.0059
Johnson, J.K. -9.0108
Johnson, J.L. -2.0040*
Johnson, L.B. -9.0013*
Johnson, N.W. -1.0058*, 2.0138*, 3.0033*, 3.0046*, 3.0103*
Johnson, R.C. -2.0039*
Johnston, M. -2.0173
Johnston, M.C. -4.0034*, 4.0052, 5.0010*
Jonck, L.M. -3.0076*
Jones, G. -15.0007*
Jordan, H.V. -1.0013*, 2.0007*
Jordan, T.H. -1.0250*, 1.0253*
Joyce, W.F. -9.0063
Jung, S. -1.0094
Junker, D.R. -1.0117
Jurand, J. -2.0169
Jussawalla, D.J. -3.0105
Kabara, J.J. -1.0210*
Kaczmarek, F. -2.0005
Kaelber, W.W. -10.0039*
Kagan, H.M. -3.0133
Kagawa, T. -11.0016
Kahn, A.J. -2.0209*
Kalkwarf, K. -10.0059
Kallenbach, E.A. -4.0064*
Kalwaic, H.J. -3.0058*
Kamath, C.R. -3.0143
Kamel, I. -9.0076
Kanapathipillai, K.R. -3.0043*
Kaplan, A. -16.0004
Kaplan, J.I. -9.0106*
Kapur, K.K. -2.0002, 4.0062*, 9.0066*
Karagianes, M.T. -9.0080
Karlsson, U. -10.0080, 10.0085
Karlsson, U.L. -10.0014*
Karon, J.M. -4.0034, 5.0010
Karsh, J. -3.0123
Kashket, S. -1.0196*, 1.0249*
Kasper, D.L. -2.0119
Katsumata, M. -5.0027, 6.0003
Katz, E.P. -2.0165*
Kauffman, D. -1.0140, 2.0086
Kaufman, S. -3.0039
Kaur, K.K. -9.0089*
Kaviani, M.J. -3.0143
Kawabata, Y. -1.0078
Kay, R.F. -4.0048*
Kaye, C. -4.0027*, 5.0008*, 6.0001*
Kayser, A.F. -9.0111
Kazandjian, G. -2.0273*
Kazimiroff, J. -1.0035
Kearney, J.F. -1.0197
Kegeles, S.S. -10.0072*
Keller, P.J. -1.0140*, 2.0086*
Kelman, A.D. -3.0133
Kelso, J.A. -4.0092
Kemp, C. -1.0157
Kemp, C.W. -1.0084, 1.0218, 1.0304
Kemp, W.B. -3.0158
Kennedy, J.E. -2.0282, 9.0119
Kenner, G.H. -9.0075, 9.0086, 9.0108
Kenny, G.E. -2.0009*
Kent, G.N. -2.0214
Keown, R.C. -9.0008
Kerr, L. -6.0012
Kerry, G. -2.0264
Kerwin, D.M. -3.0145
Kessler, L. -2.0283
Keyes, P.H. -2.0026*, 2.0271
Khosla, R. -5.0026
Kiger, R.D. -2.0062
Kim, S. -3.0142*
Kimata, K. -4.0023, 5.0031
Kimura, J.H. -1.0101, 2.0078
King, G.E. -13.0001
King, G.R. -7.0025*
King, R.E. -3.0125
Kingdon, H.S. -2.0152, 2.0245*

*INDICATES PRINCIPAL INVESTIGATOR

INVESTIGATOR INDEX

Kingman, A. -1.0022*, 1.0129, 1.0158, 1.0203*, 1.0214, 1.0258, 1.0259, 1.0260
Kirchner, J.A. -3.0079*
Kirchner, U. -1.0054*
Kiyak, A. -10.0076*
Kiyono, H. -1.0197
Klag, T.E. -11.0027*
Klavan, B. -2.0001*
Klawitter, J.J. -9.0083*, 9.0084*
Klebanoff, S.J. -2.0087
Klein, E. -1.0035
Klein, G. -3.0090
Klein, R.J. -3.0015*
Klein, R.M. -3.0138*
Kleinberg, I. -1.0144*, 1.0153*
Kleinknecht, R.A. -10.0062*
Kleinman, D. -2.0273, 10.0060
Kleinman, H.K. -2.0178*, 2.0182
Klepac, R.K. -10.0068*
Kligerman, M.M. -3.0095*
Kline, L.A. -1.0214, 1.0215, 1.0260
Klinkhamer, J.M. -2.0242
Knauer, T.E. -3.0098*
Knox, K.W. -1.0114*, 1.0115
Koback, A. -4.0054, 4.0071, 5.0052
Koch, G.G. -7.0045
Koch, W.E. -4.0012*
Koenig, H. -7.0020
Koenig, H.A. -7.0039
Kogan, K.L. -10.0067
Kokich, V. -7.0054
Kokich, V.G. -4.0029
Kolakowski, D.L. -1.0021*
Kolb, H.R. -7.0059*
Kolb, W.P. -2.0166
Kolenbrander, P. -2.0051
Kolenbrander, P.E. -2.0028*
Kollar, E.J. -2.0179*
Kolstad, R.A. -1.0005*
Konig, K.G. -15.0010*
Koopman, W.J. -1.0197
Koran, A. -9.0048*
Kornhauser, A. -3.0080
Korol, W. -9.0088
Korotzer, T.I. -2.0166
Koski, O.R. -3.0101*
Kosteic, J. -2.0278
Kotsias, J. -3.0054
Koulourides, T. -1.0063*
Kowalski, C.J. -7.0006
Krane, S.M. -2.0131
Krawczyk, W.S. -5.0014*
Kremenak, C.R. -4.0084, 5.0004
Kresch, C. -9.0078
Kresch, C.H. -9.0082
Kreutner, A. -9.0082
Krichevsky, M.I. -1.0008*, 1.0010, 2.0025*, 2.0027
Krippene, B. -12.0001*
Krischer, J.P. -6.0013*
Krishna, G. -5.0021
Kuehn, D.P. -5.0040, 5.0041
Kulhavy, R. -2.0098
Kummoona, R.K. -3.0090*
Kunyosying, U. -3.0143
Kuramitsu, H.K. -1.0109*, 1.0126*
Kurihara, S. -4.0053
Kusek, J.C. -1.0145*
Kushner, A. -1.0178
Kusy, R.P. -7.0036*, 9.0002*, 9.0003*, 9.0065*, 9.0076*
Kutscher, A.H. -15.0021*
Kuzmiak Jones, H.M. -1.0302
Labant, M.A. -9.0104
Laffer, J. -4.0001, 4.0074
Laffer, J.P. -4.0002*
Lai, C. -2.0011, 2.0019
Lai, C.H. -2.0045
Lainson, P.A. -10.0080
Lally, E.T. -2.0285
Lamberts, B.L. -1.0137*, 1.0222, 2.0187
Lancaster, W. -3.0057
Lancy, P. -2.0015, 2.0257
Lane, J.M. -1.0177
Lang, B.R. -9.0061
Langdon, J.D. -3.0046
Langeland, K. -1.0184*, 3.0160, 9.0116*
Lapeyrolerie, F. -10.0070
Laporta, R. -9.0118
Laracuente, J.M. -15.0004*
Laskin, D.M. -9.0090*, 10.0077*
Lass, J. -3.0011
Last, K. -2.0236
Latham, R.A. -7.0012
Laughlin, L.L. -13.0001
Lavelle, C.L. -9.0100*
Laven, G.T. -3.0021*
Lavker, R.M. -10.0041
Lavorato, A.S. -4.0086
Lawter, J.R. -10.0055*
Leadbetter, E.R. -2.0021, 2.0023*
Leary, L.G. -15.0020
LeBlanc, D.J. -1.0130*, 2.0284*
Lechner, J. -2.0164
Ledbetter, S. -3.0036
Le Douarin, N.M. -4.0008*
Lee, L.N. -1.0130, 2.0284
Lee, S.D. -4.0067
Lee, S.Y. -2.0240
Lee, T. -1.0102
Lee, W.A. -4.0023, 5.0031
Lees, D.E. -10.0052
LeGeros, J.P. -1.0035
LeGeros, R.Z. -1.0035*
Lehner, T. -1.0017*, 1.0307*
Leinfelder, K.F. -1.0183*, 1.0287, 9.0003, 9.0004*, 9.0057*
Lele, P.P. -15.0029
Lelievre, C. -4.0008
Lemons, J.E. -9.0053*
Lenk, E. -1.0051, 1.0052, 2.0182
Lenk, E.V. -1.0048, 2.0077, 3.0121, 3.0139, 4.0097
Lenz, H. -1.0054
Leonard, E.P. -2.0186*, 2.0187
Leonard, F. -9.0047*
Lepley, J.B. -15.0025*
leRoux, L.C. -1.0309*
Lesher, R.J. -1.0113
Leslie, B.A. -3.0117
Lester, E.P. -2.0239
Lestrel, P. -9.0066
Lestrel, P.E. -4.0062
Lettich, E. -10.0009
Levenson, G.E. -1.0252*
Leverett, D.H. -1.0229, 1.0243*, 1.0246*, 1.0317*
Levin, I. -2.0184
Levin, L.S. -6.0006*
Levine, J.D. -10.0023
Levine, M. -1.0306*, 2.0055*
Levine, M.J. -1.0120*, 3.0112, 3.0155*
Levine, M.S. -1.0120
Levinson, P.D. -2.0283
Levy, B.M. -2.0242*, 2.0261*
Levy, R.A. -10.0024*
Lewis, A.B. -4.0083
Lewis, B.S. -1.0130, 2.0284
Lewis, D.H. -9.0049, 9.0060*
Lewis, V.A. -10.0057*
Leyshon, W.C. -4.0021, 5.0019
Li, S. -1.0234*, 1.0260, 2.0165
Lian, J.B. -2.0222*
Liatukas, E.L. -1.0060*
Libbin, R.M. -4.0098
Liberman, E. -1.0004
Lichtenstein, H.A. -2.0242
Liebeskind, J.C. -10.0001
Lietze, A. -2.0203
Light, A. -10.0005
Liljemark, W.F. -1.0097*
Lillie, J.H. -2.0153, 3.0036*, 3.0106
Lin, J. -1.0066
Lin, T. -3.0011
Lindahl, R.L. -13.0008*
Linde, A. -4.0065
Linden, R.W. -10.0045*
Linder, J.E. -10.0047*
Lindhe, J.T. -2.0267*
Linsenmayer, T.F. -4.0017
Linzer, R. -1.0123*, 1.0231, 1.0296, 3.0017
Lipani, C. -15.0023
Lisker, L. -4.0092
Listgarten, M. -2.0045, 2.0108
Listgarten, M.A. -2.0011*, 2.0019*
Little, M.F. -1.0289*
Little, W.A. -1.0009*, 1.0011, 1.0085, 1.0132*, 1.0216*
Liu, C. -2.0194
Lobos, N.J. -3.0048*
Loesche, W. -2.0286
Loesche, W.J. -1.0079*, 1.0119, 1.0209*, 2.0139*
Lofqvist, A. -4.0092
Loftus, E.R. -2.0002, 2.0281
Logemann, J.A. -3.0096*, 9.0056*
Lohmander, L.S. -1.0101, 2.0078
London, J. -1.0175*, 2.0024*
Longstreth, J.D. -3.0007
Lonsdale Eccles, J. -2.0243
Lonsdale Eccles, J.D. -3.0055
Lontz, J.F. -9.0051*
Lopatin, D.E. -2.0100*
Lopez, H. -1.0164
Lorber, M. -3.0145*
Lore, J. -3.0039
Lorton, L. -3.0159
Lotzkar, S. -1.0207*
Louie, R. -1.0330*
Love, W.B. -9.0100
Lowry, W.S. -3.0071*
Lu, K.H. -1.0240*
Lucas, P. -1.0181, 2.0192
Lucas, S. -3.0045
Lucker, G.W. -10.0074
Lund, A.K. -10.0072
Lundblad, R.L. -2.0152*
Lundeen, H.C. -7.0055
Lupkiewicz, S. -7.0055, 7.0058
Lurie, A.G. -3.0052*
Luschei, E. -7.0054
Luschei, E.S. -4.0081, 10.0016*
Luton, J.G. -15.0020
Lyaruu, D.M. -1.0048, 2.0077, 4.0097
Lynch, K.L. -9.0067
Lyon, H.W. -1.0227*
Lyon, T.C. -15.0008*
Lythgoe, J.R. -3.0162
Mabie, C.P. -9.0064*
MacCallum, D.K. -2.0153*, 3.0106
Macchi, R. -9.0112
Macchi, R.L. -9.0043*
MacCulloch, W.T. -9.0113*
Macedo Sobrinho, B. -2.0112*
MacGregor, M. -1.0066
Mackenzie, I.C. -3.0028*
Mackie, P.E. -1.0036*
Mackler, B.F. -2.0109*, 2.0110, 2.0115*, 2.0120*, 2.0242
Macrina, F.L. -1.0116*
Macynski, A.A. -7.0042, 7.0049
Madero, J. -7.0042

*INDICATES PRINCIPAL INVESTIGATOR

INVESTIGATOR INDEX

Magni, F. -4.0053
Mahan, C.J. -2.0237
Mahan, P.E. -7.0055, 7.0058*
Mahler, D.B. -9.0005*, 9.0006*
Maier, D.M. -2.0029
Mailman, M.L. -2.0110, 2.0174*
Mainen, M.W. -4.0045
Majeska, R.J. -4.0094
Malhotra, S.K. -7.0019
Mancuso, D. -1.0117, 1.0124
Mandel, I. -1.0311
Mandel, I.D. -1.0019*, 1.0121, 1.0152, 1.0153
Mannel, D. -2.0128, 2.0129
Mannix, M. -3.0140
Mansheim, B.J. -2.0119*
Mante, S. -1.0125
Marantz, R.L. -9.0005
Marchetta, F. -15.0023
Marciani, R.D. -2.0231*
Marcinak, C.F. -9.0078, 9.0082
Marcus, M. -13.0006*
Marder, M.Z. -15.0021
Marek, M. -9.0009*
Markens, I.S. -4.0058*
Marker, B.C. -9.0010, 9.0024
Marker, V.A. -9.0024
Markovic, M.A. -10.0077
Marks, R.G. -7.0058
Marks, S.C. -2.0205*
Markwald, R.R. -2.0292, 4.0013
Marmai, A.R. -2.0288
Marquis, R.E. -1.0113*
Marsh, P.D. -1.0012
Marshall, G.W. -9.0010, 9.0024*
Marshall, S.J. -9.0026*
Martin, D.P. -3.0003*
Martin, G.N. -1.0049
Martin, G.R. -1.0284*, 2.0176*, 2.0177, 2.0178, 2.0182, 3.0085*, 3.0086, 4.0020*, 7.0005*
Martinez, I. -3.0039
Martinez, M.G. -15.0013*
Martinez Ross, E. -4.0093*
Martini, M.K. -2.0206
Martire, D. -2.0228, 4.0022
Mashberg, A. -3.0099*
Mason, R.M. -1.0101, 2.0078, 7.0032
Mathers, W.D. -10.0079
Mathew, M. -1.0041
Mathieson, B. -2.0125
Matz, G.J. -3.0097
Mauderli, A.P. -7.0058
May, P.D. -9.0050*
Mayer, R.M. -1.0094*
Mayne, R. -4.0065
Mazza, J.E. -2.0033
McAllister, P. -1.0102
McAllister, P.F. -1.0160
McArthur, W.P. -2.0088*, 2.0108
McCabe, M.M. -1.0095*
McCall, W.D. -7.0057*
McCarron, R.M. -2.0036
McCarthy, J. -2.0146
McCarthy, J.B. -2.0126
McCarthy, J.G. -4.0028, 4.0075, 4.0079, 4.0080
McCarty, G.A. -15.0024*
McClintock, P.R. -3.0007*
McClure, H. -4.0021, 5.0019
McClure, H.M. -5.0003*
McCoy, L.G. -11.0012*
McCoy, R.B. -13.0001
McDonald, A. -6.0014
McDonald, J.K. -2.0075*
McDonald, M. -10.0068
McDowell, T. -1.0110
McGaughey, C. -1.0072*, 1.0073, 3.0089*
McGhee, J.R. -1.0138*, 1.0197*, 2.0098, 3.0021
McGrath, P.A. -10.0049*, 10.0051*
McIntire, F.C. -1.0082*, 2.0028, 2.0046, 2.0051
McKelvy, B.D. -2.0157
McKenna, T.M. -10.0004, 10.0005, 10.0006
McKenna, T.W. -1.0018*
McKinney, R. -1.0011
McKinney, R.V. -4.0088*
McKusick, V.A. -6.0006
McNamara, J.A. -4.0041*, 4.0090*, 7.0043*, 7.0047
McNamara, T.F. -2.0107
McNee, S.G. -2.0035
McNulty, W.P. -6.0002*
McWilliams, R.W. -3.0120*
Mealiea, W.L. -10.0063
Mechanic, G.L. -2.0160*, 2.0161*
Medlin, T.P. -1.0178*, 1.0179*, 10.0031, 10.0033
Meenaghan, M.A. -2.0247, 9.0081, 15.0023
Meeuwissen, R. -9.0111*
Mehta, F.S. -3.0049*, 3.0065*, 3.0066*, 3.0104*
Mei, C. -10.0046*
Meier, S.P. -4.0014*, 4.0016*
Melamed, B.G. -10.0064*
Meller, S.M. -5.0015*
Mellonig, J.T. -2.0185*
Melnick, M. -5.0002, 5.0005, 5.0024
Menaker, L. -1.0163*
Mengoli, H.F. -2.0141*
Mercer, P. -1.0010, 2.0027
Merchant, H.W. -3.0153*
Mergenhagen, S.E. -2.0129, 2.0132
Merritt, A.D. -3.0134
Messer, H.H. -2.0249*
Mestecky, J.F. -2.0098*
Metzger, Z. -2.0130, 2.0133
Meyer, J. -3.0081*
Meyer, J.L. -1.0051*
Meyer, M.W. -3.0157*
Meyers, R. -1.0277, 1.0279, 1.0283
Meyers, R.J. -1.0258, 1.0281*
Michalek, S.M. -1.0197, 2.0132
Michelich, R.M. -1.0024*
Mikulski, A. -2.0203
Miles, A.E. -2.0148*
Milgrom, P. -13.0003, 13.0007*, 16.0003*
Miller, A.J. -1.0201, 4.0091*, 7.0009, 7.0013
Miller, A.S. -15.0022*
Miller, C.H. -2.0003*, 2.0274
Miller, D. -7.0038
Miller, E.J. -2.0163*
Miller, G. -2.0103
Miller, I.J. -10.0022*
Miller, R.A. -11.0011*
Miller, R.L. -15.0017
Miller, S.C. -2.0225*
Miller, W.A. -1.0065, 7.0001*, 9.0115*
Millikovsky, W.G. -4.0034, 5.0010
Minah, G.E. -1.0083*
Mincer, H.H. -3.0101
Minix, K. -9.0109
Minkin, C. -2.0213*
Minkoff, R. -4.0052*
Minkoff, R.M. -4.0034, 5.0010
Mirth, D.B. -1.0129*, 1.0260, 1.0305
Misra, D.N. -9.0021
Mistretta, C.M. -4.0010*, 4.0073
Mitchell, R. -9.0015
Mitchem, J.C. -9.0005, 9.0042
Mitoma, C. -1.0193*
Miyamoto, M.S. -1.0048, 2.0077, 4.0097
Miyares, J.H. -1.0219*
Mizel, D. -2.0131, 2.0134
Mizel, S. -2.0125, 2.0128
Mizel, S.B. -2.0131*, 2.0134*
Moffa, J.P. -9.0030*
Moffett, B.C. -4.0029, 4.0081, 7.0054*
Moffitt, F.H. -4.0076
Mohl, N.D. -7.0057
Molnar, S. -12.0003*
Molthen, R. -4.0076, 7.0038
Molyneux, M. -3.0045
Monat, R.K. -5.0051
Monell Torrens, E. -1.0159, 1.0194, 1.0303
Montes, M. -2.0093, 3.0088
Montgomery, E.H. -2.0004*
Montgomery, P.C. -2.0285*
Moore, B.K. -9.0059
Moore, J.R. -9.0096*
Moore, R. -2.0125, 2.0129
Moore, R.N. -2.0132*.
Moore, R.R. -9.0086
Moore, W.E. -2.0014*, 2.0020
Moorrees, C.F. -7.0017*
Mooser, G. -10.0010*
Morahan, P.S. -3.0018
Moreno, E.C. -1.0064*
Morgan, P.R. -5.0020*
Morhart, R.E. -1.0213*, 1.0312*
Moriarty, J.D. -2.0173
Moriarty, M.N. -3.0067
Morita, Y. -2.0124
Morris, H.F. -9.0068*
Morris, H.L. -5.0004*, 5.0040*, 5.0041*, 5.0047*
Morrison, D.J. -2.0141
Morrison, E. -2.0264
Morrison, M. -1.0146
Morton, J. -7.0039
Moschera, J. -3.0053
Moskowitz, H.D. -9.0025*
Moss, J.P. -7.0028
Moss, M.L. -4.0043*
Motohashi, N. -5.0045
Moutsopoulos, H. -3.0006
Moutsopoulos, H.M. -3.0123*
Moyers, R.E. -4.0039*, 10.0074
Moyle, D.O. -9.0108
Mozden, P. -15.0029
Mueller, R. -10.0034
Mueller, W.J. -2.0208
Muhl, Z.F. -7.0022*
Mukherjee, A.K. -3.0102*
Muller, T. -9.0059
Muller, T.P. -7.0012, 7.0041
Muller, V. -2.0289
Mullins, R. -16.0004*
Mulvihill, J.E. -2.0168
Munger, B. -4.0045
Munson, P.L. -2.0195
Munzenmaier, A. -2.0005
Murayama, D. -4.0045, 4.0054, 4.0071, 5.0052
Murphy, E.A. -6.0006
Murphy, R.C. -1.0082
Murray, B. -16.0004
Murray, B.K. -3.0018*
Murray, E. -1.0286, 2.0191
Murray, J.C. -2.0176, 2.0178, 3.0085, 4.0020, 7.0005
Murray, J.G. -14.0003
Myers, B.R. -9.0086
Myers, E. -15.0028
Myers, M. -9.0078, 9.0082
Mylin, W.K. -5.0051

INVESTIGATOR INDEX

Nagel, R.N. -1.0187, 1.0188, 2.0269, 2.0270, 4.0078
Nahmias, A.J. -3.0029*, 3.0132
Nair, P.N. -3.0072
Nancollas, G.H. -1.0065*
Nanda, C.R. -9.0020
Nanda, R. -7.0050*
Narayanan, A.S. -2.0094, 2.0166
Narayanan, M. -3.0042*
Nasjleti, C.E. -2.0155, 4.0031*, 7.0052*, 9.0122*
Natiella, J.R. -2.0247*, 9.0081*, 15.0023
Navia, J.M. -1.0164*, 1.0291, 2.0059*
Navia, M. -1.0046, 2.0076
Naylor, -13.0013
Neiders, M.E. -2.0154*
Neiman, A. -1.0028
Nelson, J. -8.0003
Nelson, J.F. -3.0001, 8.0002, 11.0006, 11.0009*
Nery, E.B. -2.0276, 9.0067*
Neshat, A.A. -3.0148*
Neumann Jensen, B. -3.0075
Neumann Jensen, B.L. -3.0062
Nevins, A.J. -9.0118*
Newbrey, J.W. -2.0224*
Newbrun, E. -1.0075*
Newbury, D.E. -1.0045*
Newcomb, R.W. -1.0295*
Newesely, H. -1.0054, 9.0044
Newman, G.V. -9.0039
Newman, H.N. -2.0034*
Newman, M.G. -2.0030, 2.0033, 2.0044*
Newsome, D. -4.0030, 5.0038
Newsome, J.F. -15.0015*
Nicholls, J.I. -4.0081
Niebyl, J. -5.0023*
Niederman, R. -2.0272, 4.0055*, 11.0029*
Niederpruem, D.J. -2.0003
Nikias, M.K. -1.0311*
Nikodem, V. -1.0046, 2.0076
Nilsson, B. -1.0101, 2.0078
Nilsson, U.R. -2.0096*, 2.0108, 2.0116*
Nimni, M. -2.0203
Nisengard, R.J. -1.0294*, 2.0105*
Nissle, R. -2.0264
Nord, S.G. -10.0040*
Norling, B.K. -9.0109*
Norman, M.E. -2.0096, 2.0108, 2.0116
Norr, S.C. -4.0015*
Northington, L. -10.0070
Northoff, H. -2.0125
Norton, L.A. -4.0094
Nossal, R.J. -2.0080
Notani, P.N. -3.0041, 3.0105*
Notkins, A.L. -3.0005, 3.0006, 3.0007, 3.0037, 3.0057, 3.0122*
Novak, J.E. -1.0103*
Nowotny, A. -2.0097*
Nowotny, A.H. -2.0045*
Nowotny, A.M. -2.0045
Nuki, K. -2.0092, 2.0211*
Nye, P.W. -4.0092
Nygaard, V.K. -1.0027
O'Brien, A. -2.0135
O'Brien, W.J. -1.0030*, 1.0186*
Occhino, J.C. -3.0106*
Ochiai, K. -1.0078
Ogletree, F.F. -2.0162
Oguchi, H. -2.0215
Oguntebi, B. -9.0116
Oka, S.W. -5.0037*
Okabe, T. -9.0015*
O'Keefe, E.M. -3.0158
O'Keefe, T.J. -1.0226*
O'Leary, T.J. -2.0274
Oleson, T.D. -10.0021
Oliet, S. -9.0117*
Oliver, C. -3.0121, 3.0139*
Oliver, L.K. -1.0114, 1.0115
Olsen, C.E. -2.0146
Olson, C. -3.0057
Olson, D. -2.0125
Olson, J.A. -3.0035
Olson, R.E. -10.0077
Olsson, B.E. -9.0116
O'Neill, P.A. -2.0110*, 2.0115, 4.0096
Ono, K. -1.0093
Onodera, T. -3.0122
Opderbeck, W.R. -2.0268*
Openshaw, H.O. -3.0005*
Ophaug, R.H. -1.0024, 1.0181, 1.0266, 1.0267*, 1.0268, 1.0269*, 1.0270, 1.0271, 1.0272, 1.0273, 1.0286, 2.0180, 2.0190*, 2.0191, 2.0192
Oppenheim, F.G. -3.0112, 3.0133*
Oppenheim, J. -2.0129, 2.0130
Oppenheim, J.J. -2.0125*, 2.0132, 2.0133
Orkand, P.M. -3.0119
Orkand, R.K. -3.0119
Orkin, R.W. -4.0006, 4.0017*
Osdoby, P. -2.0206
Osetek, E.M. -13.0001
Osterberg, S.K. -2.0094
Otomo, J. -3.0150
Otomo, J.A. -2.0280
Oudhof, H.A. -4.0058
Ouellette, L.A. -2.0177, 3.0086
Outhwaite, W.C. -9.0017*
Overall, J.C. -3.0002*
Overberger, C.G. -9.0014
Oyen, O.J. -4.0046*
Paffenbarger, G.C. -9.0019
Page, R.C. -2.0094, 2.0166*
Paglia, L.M. -2.0177*, 3.0086*
Palcanis, K.G. -2.0020
Palenik, C.J. -2.0003
Palla, S. -7.0053
Palma, M. -10.0077
Papierman, S.K. -4.0098
Paquette, O. -9.0114
Paradise, J.L. -5.0048
Park, J.B. -9.0075*, 9.0086*, 9.0108
Park, M. -1.0020
Parker, J. -1.0309
Parmley, R.T. -2.0099*
Parnaik, V. -1.0094
Parris, P. -4.0001, 4.0002, 4.0074
Pashley, D.H. -1.0033*
Pass, F. -3.0057
Passo, S. -2.0108
Patel, D.D. -3.0047*
Paterson, R.C. -1.0189*
Patrucco, R.A. -3.0021
Patters, M.R. -2.0212
Patthoff, D.E. -2.0277*
Paulson, R.B. -1.0053*
PavanLangston, D. -3.0011
Pavlidis, N. -3.0123
Payne, T. -3.0001
Paz, M. -2.0193
Pazin, G.J. -3.0008
Pazoles, P.P. -2.0145
Pearsall, N.N. -3.0026*
Peavy, D.L. -3.0023*
Peckauskas, R. -1.0068
Peckauskas, R.A. -1.0071
Pelleu, G.B. -13.0001*
Pellissier, J.F. -6.0009
Penas, L. -5.0008, 6.0001
Pennypacker, J.P. -2.0182, 4.0023*, 5.0031*
Pentel, L. -1.0035
Perez, P. -9.0066
Peri, B.A. -1.0299*
Person, P. -2.0273, 4.0098*, 10.0060
Peskin, B. -9.0116
Peters, B.A. -2.0109
Peters, D.D. -3.0159*
Peters, E.H. -3.0134
Peterson Falzone, S.J. -5.0042*, 7.0030*
Petrin, P. -1.0236
Pfaffenbach, H. -9.0024
Phillips, R.W. -1.0255*, 9.0016*
Philpott, G. -15.0014
Pickren, J.W. -15.0023
Picton, D.C. -2.0081*, 7.0028*
Pierce, R.H. -4.0045
Pieringer, R.A. -1.0173*
Piez, K.A. -1.0046, 2.0076, 2.0080
Pindborg, J.J. -3.0062, 3.0063*, 3.0066, 3.0075*, 3.0093*, 3.0104
Pink, T.C. -1.0209
Plasschaert, A.J. -15.0010
Plata, R.L. -2.0062
Pliskin, M.E. -3.0056*
Plunka, S.M. -2.0133
Poe, P.R. -10.0004
Point, D.D. -3.0064
Polissar, L. -3.0038*
Pollock, J.J. -1.0148*
Polson, A.M. -7.0035*
Poole, R. -1.0101, 2.0078
Porter, E.V. -1.0128
Porter, K. -2.0234, 2.0235
Porter, T. -1.0046, 2.0076
Posey, W.R. -11.0009
Posner, A.S. -1.0177
Povlishock, J.T. -3.0018
Powell, J.T. -2.0036
Powers, J.M. -9.0007*
Powers, K.J. -1.0178, 10.0033
Praetorius, F. -3.0092*
Pratt, N.E. -3.0116
Pratt, R.M. -4.0021*, 4.0024, 5.0019*, 5.0020
Preston, J.D. -9.0031*
Preti, G. -2.0278
Price, S. -4.0069*
Pring, M. -6.0012
Priotto, E.G. -9.0036, 9.0112
Proffit, W. -7.0046
Proffit, W.R. -7.0045*
Proudfit, H.K. -10.0024
Proust, J.P. -2.0149*, 4.0050*
Prunes, N. -4.0061
Prusoff, W.H. -3.0011
Pruzansky, S. -4.0001*, 4.0002, 4.0027, 4.0074*, 5.0006, 5.0007, 5.0045*, 6.0010*, 7.0015, 7.0016
Pryputniewicz, R.J. -7.0020
Puga Carrasco, A. -3.0005, 3.0057
Pullman, I. -1.0068*, 1.0071*
Pullon, P.A. -2.0223, 15.0014*
Putney, J.W. -3.0117*
Pyeritz, R.E. -6.0006
Quirolgico, G. -1.0035
Quissell, D.O. -3.0154*
Qwarnstrom, E.E. -3.0121
Rabadjija, L. -2.0193
Rafferty, D.M. -2.0136*
Raft, D. -10.0008
Raghavan, S. -1.0066
Raisz, L. -2.0145
Ramamurthy, N.S. -2.0168
Ramfjord, S.P. -2.0252, 2.0264*, 7.0027
Ramp, W.K. -2.0199, 2.0291
Rand, J.H. -5.0051
Rand, K.H. -3.0031*
Randeria, J.D. -3.0068*, 3.0091*
Ranney, R.R. -2.0020*, 2.0111*
Rao, G.S. -6.0005*, 10.0056

*INDICATES PRINCIPAL INVESTIGATOR

INVESTIGATOR INDEX

Rao, R.S. -3.0072
Rao, S.M. -10.0075
Rapaport, F.T. -4.0028, 4.0079
Rapidis, A. -3.0046
Rasmussen, H. -2.0210*
Ratches, J. -7.0039
Ratener, P. -10.0067, 10.0076
Rath, N.C. -2.0228, 4.0022
Ratner, E. -10.0060*
Rattner, S.L. -1.0049
Raubenheimer, E.J. -3.0076
Raupp, L. -2.0125
Rawls, H.R. -1.0230*
Reddi, A.H. -2.0228*, 4.0022*
Reddy, J. -1.0089*
Redman, R.S. -3.0114*, 3.0124*
Reed, M.J. -2.0117*
Reese, J.A. -1.0187, 2.0269
Reese, S. -9.0008
Reger, R.H. -1.0325*
Reilly, J.A. -1.0102
Reisbick, M.H. -9.0031, 9.0032*
Reith, E.J. -1.0034*
Rennard, S.I. -2.0176, 3.0085, 4.0020, 7.0005
Retief, D.H. -1.0228*
Reusch, V.M. -2.0042*
Revis, G. -2.0051
Revis, G.J. -2.0022, 2.0046*
Reynolds, J.J. -4.0060*
Reynolds, P.J. -10.0013*
Rhodes, R.K. -2.0163
Ribas, L.M. -9.0043
Rice, D.H. -11.0026*
Rice, R.W. -4.0046
Richardson, B.A. -9.0124*
Richardson, E.R. -7.0019*
Richardson, J. -15.0029
Richeimer, W. -3.0161
Richter, M. -7.0029*
Ricks, C.L. -2.0062*
Riedner, E.D. -6.0006
Rifkin, B.R. -2.0251*
Rinard, G. -3.0132
Ringle, R.D. -9.0058
Ringleberg, M. -1.0257*
Rins de David, M.L. -3.0126*, 3.0127
Ripa, L.W. -1.0247*, 1.0315*
Riviere, G.R. -9.0121*
Roberts, W.E. -7.0060*
Robertson, P.B. -2.0212, 2.0242
Robey, P.G. -2.0176, 3.0085, 4.0020, 7.0005
Robinovitch, M. -3.0109
Robinovitch, M.R. -1.0141*, 2.0056*
Robinson, C. -1.0056*, 1.0057*, 1.0074, 1.0191*
Robinson, T.C. -9.0081
Robinson, W. -15.0027
Robrish, S.A. -1.0084*, 1.0218, 1.0304*, 1.0305
Robson, M.C. -3.0097*
Robyt, J.F. -2.0043*
Roche, A.F. -4.0083*
Roche, M. -1.0170
Rodan, G.A. -4.0094*
Roden, L. -2.0181*
Rodgers, P. -1.0158
Rodrick, M. -2.0114
Roeber, F. -7.0040
Roed Petersen, B. -3.0063, 3.0093
Rogers, A.H. -1.0016*
Rogers, R.S. -3.0024*
Rokaw, E. -1.0128
Rolince, D.E. -10.0040
Rolla, G. -1.0102
Rolla, R. -10.0067
Rollnick, B. -4.0027
Rooney, G.E. -9.0067
Rosan, B. -2.0015*, 2.0257*
Rose, G.G. -2.0237*
Rosen, M.S. -9.0056
Rosenbloom, J. -2.0068*
Rosenfeld, J.P. -10.0020*
Rosenstreich, D.L. -2.0129*, 2.0135*, 3.0010*
Ross, G.S. -10.0040
Ross, J.R. -2.0219
Rosse, C. -2.0142
Rossiwall, B. -9.0044*
Rossomando, E.F. -4.0025*, 4.0026*
Roth, G.I. -2.0231
Rovelstad, G. -1.0122
Rover, B.C. -2.0283*
Rowe, N.H. -3.0013
Rozanis, J. -11.0028
Rubick, N.F. -1.0178
Ruda, M.T. -10.0036*
Rupp, N.W. -9.0019*
Ruscello, D.M. -5.0050
Russell, E.A. -8.0003*, 9.0101
Russell, M.P. -3.0040
Rustioni, A. -10.0004
Rutberg, M.H. -9.0116
Rutherford, R.B. -2.0122*
Ryan, D. -15.0027
Ryan, V.W. -1.0121, 1.0154*
Ryge, G. -9.0018*
Sabes, W.R. -15.0016*
Sadowsky, C. -7.0033*
Safavi, K.E. -9.0116
Sakamoto, M. -2.0215
Sakamoto, S. -2.0193, 2.0215*
Salomon, D.S. -4.0021, 5.0019
Saluk, L.W. -1.0186
Sammon, P.J. -2.0217*
Samuels, L. -7.0037
Sandberg, A. -3.0006
Sandberg, A.L. -2.0145*, 2.0146
Sando, J.J. -2.0131
Sanford, C. -13.0005
Sanghvi, L.D. -3.0041, 3.0105
Sanguiolo, R. -11.0020*
Sannazzari, G.L. -3.0060
Sansone, F.M. -3.0121
Sapperstein, S. -4.0054, 4.0071, 5.0052
Saris, W.H. -15.0010
Sarkar, N.K. -9.0020*
Sarnquist, F.H. -10.0079*
Sasmore, D.P. -1.0193
Sassouni, V. -4.0077*, 7.0051*
Savara, B.S. -10.0082*
Scaletta, L.J. -3.0106
Schaaf, N.G. -15.0023
Schachtele, C.F. -1.0032*, 1.0127
Schaefer, R.H. -1.0322*
Schaeffer, L.D. -3.0150
Schallhorn, R.G. -2.0232*
Schechter, A.N. -1.0050, 2.0079
Schechter, G. -2.0125, 2.0133, 2.0146
Schemmel, R. -1.0210
Schenkein, H. -2.0103
Schiffman, S. -2.0265
Schiffmann, E. -2.0289*
Schiller, R. -1.0121*, 1.0154
Schlenker, J.D. -3.0097
Schlesinger, D.H. -1.0151*
Schmidt, R. -9.0054*
Schneider, G.B. -2.0216*
Schneir, M.L. -2.0167*
Schnell, R.J. -1.0255
Schneyer, C.A. -3.0131*
Schnitman, P. -9.0079
Schnitman, P.A. -9.0085*
Schoenberg, B. -15.0021
Schoenfeld, C.M. -9.0059
Schofield, I.D. -11.0028
Schon, M. -4.0045
Schonfeld, S.E. -2.0118*
Schraer, H. -2.0202*, 2.0208*
Schreiner, R.R. -10.0006
Schrode, J. -2.0239
Schuette, W.H. -1.0233
Schull, W.J. -7.0006
Schutzbach, J. -2.0181
Schwabe, C. -2.0075
Schwartz, J. -15.0031
Schwartz, S.A. -4.0066*
Schweiger, J.W. -9.0051
Schweizer, G. -4.0008
Scopp, I. -2.0241
Scopp, I.W. -2.0275*, 9.0091*
Scott, D.F. -2.0037
Scott, D.M. -2.0214
Scott, J.N. -1.0028
Scott, R. -15.0028
Searls, J.C. -5.0004
Sector, I. -10.0077
Seelig, G.F. -2.0239
Segrest, J.P. -2.0058*
Segreto, V.A. -1.0285
Seibel, H.R. -7.0004
Sekizawa, T. -3.0005
Seliger, W.G. -4.0013*
Selinger, H.A. -1.0051
Seltzer, Z. -10.0032
Selvig, K.A. -2.0017*
Senseman, D.M. -3.0119*, 7.0026*, 10.0041
Serling, J. -13.0004, 13.0005
Sessle, B.J. -10.0001, 10.0015*
Setterstrom, J. -11.0033
Shaffer, E. -3.0057
Shah, K. -3.0057
Shah, R.M. -5.0032*
Shanfeld, J.L. -7.0003
Shannon, I.L. -1.0262*, 3.0149*
Shapiro, B.H. -5.0027
Shapiro, E. -7.0040*
Shapiro, I. -11.0035*
Shapiro, I.M. -2.0070*
Shapiro, P. -4.0081, 7.0054
Sharon, I.M. -3.0141
Shaw, R.E. -4.0082*
Shearer, T.R. -1.0031*, 1.0039, 1.0040*, 1.0288*
Shedd, D. -3.0039
Shedd, D.P. -3.0040, 15.0023
Sheetz, J.H. -3.0111*, 4.0065
Shelton, R.L. -5.0050*
Sherman, C. -1.0327*
Shern, R.J. -1.0214*, 1.0215*, 1.0233*, 1.0260*, 1.0305
Shetlar, M.R. -2.0292
Shields, E.D. -5.0002
Shigeto, A. -2.0146
Shikes, R. -15.0027
Shimizu, F. -3.0007
Shiota, T. -1.0078*, 1.0206*
Ship, I. -11.0035
Shipman, B. -15.0020
Shipman, C. -3.0013
Shklair, I.L. -1.0137, 1.0204*, 1.0239*, 2.0186
Shklar, G. -3.0032*, 3.0080*, 15.0031*
Shnorhokian, I. -7.0051
Shockman, G.D. -1.0110*
Shovlin, F.E. -1.0172*
Shroff, B.C. -3.0065
Shulman, L.B. -9.0079*
Shyu, K. -1.0169*
Siegel, I. -3.0109
Siegel, J. -1.0004
Siegel, M.I. -4.0051

*INDICATES PRINCIPAL INVESTIGATOR

INVESTIGATOR INDEX

Siegel, R.L. -3.0161
Sierra, -1.0158
Siervogel, R.M. -4.0083
Siew, C. -2.0290*
Silva, J.A. -1.0224
Silver, M. -4.0021, 5.0019
Silverman, S. -15.0011*, 15.0012*
Silversin, J.B. -1.0329*, 10.0087
Silverstein, S.J. -1.0323*
Silverstone, L. -1.0202
Silverstone, L.M. -1.0150*, 1.0254
Sim, R. -4.0021, 5.0019
Simmelink, J.W. -1.0027*
Simmons, D.J. -2.0209
Simon, J.H. -2.0147*, 3.0162*
Simonson, L.G. -1.0222*
Simpers, N. -2.0283
Simpson, D.M. -3.0136
Simpson, J.W. -2.0238*, 2.0242
Simpson, M. -6.0014
Simpson, R. -1.0202
Sims, T.N. -2.0030*, 2.0032, 2.0033*, 2.0157*, 2.0183*, 2.0280*, 2.0287*, 3.0150*, 10.0081*
Singer, L. -1.0024, 1.0181*, 1.0265*, 1.0266*, 1.0267, 1.0268, 1.0269, 1.0270*, 1.0271*, 1.0272*, 1.0273, 1.0286*, 2.0180*, 2.0190, 2.0191*, 2.0192*
Singer, R.M. -5.0016
Singh, B. -2.0037, 3.0019, 3.0137*
Singh, B.B. -4.0088
Singh, S. -1.0212
Sipe, J.D. -2.0129
Siraganian, R. -2.0124*, 2.0127*, 2.0130
Siraganian, R.B. -3.0006
Sist, T. -2.0093*
Sist, T.C. -3.0088*
Sivayoham, S. -3.0069*
Skalabrin, N. -16.0003
Skinner, D.E. -1.0244*
Skobe, Z. -1.0037*
Skolnick, M.L. -5.0049
Slack, G.L. -1.0012*
Slade, H.D. -1.0111*
Slavkin, H.C. -4.0003*, 4.0005*, 5.0005*, 5.0024*
Slee, A.M. -2.0038*
Small, E.W. -10.0085
Smibert, R.M. -2.0014, 2.0020
Smith, C.D. -9.0058
Smith, C.E. -1.0044*
Smith, C.J. -2.0158*
Smith, C.T. -1.0285*
Smith, D. -2.0101
Smith, D.C. -9.0124
Smith, D.J. -1.0297, 2.0106
Smith, E. -2.0228, 4.0022
Smith, E.E. -1.0093*
Smith, F.N. -2.0100
Smith, G.M. -10.0078*
Smith, J. -4.0008
Smith, J.C. -1.0165
Smith, K. -2.0125
Smith, N.J. -3.0143
Smith, O.A. -4.0029*
Smith, Q.T. -1.0127
Smith, R.A. -10.0023
Smith, W.N. -2.0242
Smithies, O. -3.0134
Smuts, M.E. -5.0018*
Snyder, A.J. -11.0010
Snyder, J.M. -2.0277
Snyder, W.H. -9.0039*
Snyderman, R. -2.0091*
Socransky, S.S. -2.0008*, 2.0012*, 2.0016*, 2.0265*
Sodicoff, M. -3.01[illegible]6*
Solomon, L.M. -4.0087*
Solonche, D.J. -7.0039
Solt, D.B. -3.0080
Sonawane, B.R. -6.0003
Soni, N.N. -2.0188*, 7.0008*
Sonis, S.T. -2.0114*, 15.0031
Sorgente, N. -4.0035*
Sorin, S.M. -9.0117
Soskolne, A. -2.0211
Soto, E. -15.0029
South, R.J. -1.0012
Spangberg, L.S. -9.0116
Spangenberg, D.B. -1.0042*
Specter, S.C. -3.0020*, 3.0022*
Spector, M. -9.0078, 9.0082*
Spector, P.C. -1.0038
Spencer, H. -2.0204*
Sperber, G.H. -7.0007*
Spitz, L.K. -11.0035
Squier, C.A. -4.0084
Staat, R.H. -1.0098*
Stahl, S.S. -2.0241, 9.0091
Stanford, J.W. -9.0103*
Stapleton, M.F. -9.0005
Starr, P. -10.0073*
Stashenko, P. -2.0101*
Stashenko, P.P. -2.0106
Staz, J.F. -3.0044
Steeg, P.S. -2.0132
Steel, M. -1.0067
Steven, A. -1.0046, 2.0076
Stevens, R.H. -1.0107
Stevens, R.L. -1.0101, 2.0078
Sticht, F.D. -2.0219
Stiles, H.M. -1.0280*, 1.0282*, 1.0305
Stinson, M.W. -1.0092*, 2.0105
St. Martin, E.J. -1.0099, 1.0130, 1.0131*, 2.0284
Stoller, N.H. -1.0215, 2.0108
Storb, U.B. -2.0095*
Stowell, E. -1.0072, 1.0073*, 3.0089
Stradley, A.L. -2.0028
Strauss, R.P. -13.0008
Streckfuss, J.L. -1.0211, 2.0242
Streko, T. -10.0050, 10.0071
Strong, S. -15.0029
Strosberg, A.M. -1.0161
Stupp, S.I. -9.0028*
Subba Rao, G. -1.0173
Sudarsanan, K. -1.0026
Suddath, F.L. -1.0062
Suddick, R.P. -1.0098
Sulik, K.K. -5.0017*
Sullivan, T. -4.0055
Sullivan, T.M. -2.0272*, 9.0094
Sullman, S. -2.0165
Sultz, H.R. -3.0040
Summers, C.J. -10.0074
Sumner, A.J. -11.0035
Sun, H.S. -2.0240
Sutter, V.L. -2.0031*, 2.0032*
Sutton, R.B. -2.0138
Svanberg, G. -2.0264
Swango, P.A. -1.0234, 1.0259
Swartz, M.L. -1.0255
Sweeney, E.J. -9.0033*
Sweet, J.B. -7.0042*, 7.0049*, 10.0050, 10.0071
Syed, S.A. -2.0139
Syftestad, G. -2.0203
Szabo, E.I. -2.0049
Szabo, G. -2.0150*, 2.0226, 5.0014
Szwejda, L.F. -1.0319*
Tabak, L.A. -1.0120
Taichman, L.B. -4.0011*
Taichman, N.S. -2.0088, 2.0108*
Takagaki, Y. -4.0006
Takagi, S. -1.0041
Talal, N. -3.0035
Talbot, T.L. -1.0233
Tamarin, A. -3.0109, 4.0038*
Tandler, B. -3.0106
Tanner, A. -2.0012
Tanner, S.F. -13.0008
Tanzer, J.M. -1.0171*, 1.0298*, 2.0038
Tashjian, A.H. -2.0193
Taubman, M. -2.0101
Taubman, M.A. -1.0104*, 1.0297*, 2.0106*
Taylor, B. -2.0135
Taylor, B.A. -3.0007
Taylor, D.F. -2.0196*, 9.0002, 9.0057, 9.0077*
Taylor, K.G. -1.0212
Taylor, R. -1.0163
Taylor, S.A. -1.0179, 10.0033*
Teeter, J.H. -10.0041
Teillet, M. -4.0008
Teitelbaum, S.L. -2.0223
Telser, A.G. -5.0001
Termine, J.D. -1.0048*, 2.0077*, 4.0097*
Terrill, A.J. -1.0320*
Terry, B. -7.0032
Terry, B.C. -10.0085
Tew, J.G. -2.0103*, 3.0018
Thaller, B. -2.0275
Thayer, H. -11.0016*
Theophel, S.M. -10.0073
Thesleff, I.P. -4.0021, 5.0019
Thibodeau, E.A. -1.0113
Thomas, D.B. -3.0038
Thomas, E.L. -1.0146*
Thomas, J.P. -1.0318*
Thompson, H. -10.0079
Thompson, K.R. -9.0070*
Thompson, V.P. -9.0011*
Thomson, L.A. -1.0009, 1.0011*, 1.0085*, 1.0132, 1.0216, 1.0305
Thomson, P.L. -1.0012
Thorpe, J.D. -2.0001
Tinanoff, N. -1.0221*, 1.0238*
Todaro, F.J. -2.0134
Toga, C.J. -1.0224*
Tomer, B. -7.0009
Tomich, P. -1.0208
Toniolo, A. -3.0122
Tonn, E.M. -9.0018
Toolan, H.W. -6.0004*
Toole, B.P. -4.0006*, 4.0017
Torabinejaad, M. -3.0162
Torchia, D.A. -1.0050*, 2.0079*
Toverud, S.U. -2.0195*, 2.0199*, 2.0291*
Tow, D.E. -2.0272, 4.0099
Townsend, G.C. -12.0005
Tozer, R.S. -3.0045
Triplett, R.G. -8.0004*, 8.0005*
Truelove, E. -3.0144
Truelove, E.L. -3.0027
Truin, G.J. -15.0010
Trummel, C.L. -2.0212*
Trus, B.L. -1.0046*, 2.0076*
Tryggvason, K. -2.0176, 3.0085, 4.0020, 7.0005
Tsai, C. -2.0088, 2.0108
Tsaknis, P. -9.0101
Tschamer, H. -1.0236*
Tso, H. -9.0056
Tsukamoto, Y. -2.0126
Tung, M. -1.0070
Turgeon, L. -1.0311
Turner, C.G. -12.0004*
Turner, D.T. -1.0287*, 2.0244*, 9.0002, 9.0102*
Turner, G. -1.0014

*INDICATES PRINCIPAL INVESTIGATOR

INVESTIGATOR INDEX

Turner, G.E. -10.0080
Turriff, C. -5.0008, 6.0001
Turvey, T.A. -5.0044, 7.0031, 7.0045
Tuttle, R.H. -7.0012
Tyan, M.L. -5.0035*, 5.0039*
Tyler, M.S. -4.0018*
Underhill, C.B. -4.0006
Unver, S. -3.0070
Uribe, E.J. -9.0036*, 9.0112*
Uribe, E.N. -9.0036
Urist, M.R. -2.0203*
Uthman, A.A. -7.0057
Uzzell, B. -11.0035
Vaidyanathan, T.K. -9.0029*
Vail, M.S. -2.0163
Van Demark, D.R. -5.0040
Vanderdonck, R.J. -15.0003
van Houte, J. -1.0106*, 2.0006*
Vann, W.F. -15.0002*
van Palenstein Helderman, W.H. -1.0023
van Veen, M. -15.0010
van Wyk, C.W. -1.0089, 1.0090, 1.0309, 3.0044*, 3.0077*
Vargervik, K. -4.0091, 7.0009, 7.0037
Varner, H. -4.0023, 5.0031
Vatessari, G.T. -1.0273*
Vatter, A.E. -1.0082, 2.0022, 2.0046, 2.0051
Vazquez Cabrera, C. -3.0005
Veis, A. -2.0164*
Venham, L.L. -10.0048*
Venkatasubramanian, K. -2.0289
Verbin, R.S. -15.0028*
Vercellino, V. -3.0060
Verdier, M. -1.0067
Vermilyea, S. -9.0001
Vermilyea, S.G. -11.0008, 11.0034
Verrusio, A.C. -7.0041, 10.0056*
Vieras, F. -8.0004
Vig, P.S. -7.0032*, 7.0045
Vignery, A. -2.0210
Vignon, C. -2.0149, 4.0050, 6.0009*
Virolainen, K.M. -7.0012
Vlagopoulos, T. -2.0124
Vogel, G.L. -1.0067
Vogel, J.J. -1.0081*, 2.0242, 4.0096
Vogel, S.N. -2.0129
Vogels, A.L. -15.0010
von Recum, A. -9.0086
von Recum, A.F. -9.0075, 9.0108
Wada, T. -4.0084*
Wagenknecht, K. -9.0116
Wagner, R. -1.0187, 2.0269
Wahl, L. -2.0129
Wahl, L.M. -2.0126, 2.0132, 2.0145, 2.0146*
Wahl, S. -2.0129
Wahl, S.M. -2.0126*, 2.0130, 2.0146
Wahn, H.U. -2.0124
Walczak, C.A. -1.0010*, 2.0027*
Waldron, C.A. -15.0019*
Walker, B.E. -5.0012*
Walker, C. -2.0012
Walker, D.M. -2.0085*
Walker, G.F. -7.0006
Wall, J. -2.0080
Wallenstein, S. -1.0020
Walsh, J.M. -8.0005
Walters, P.L. -2.0253*, 2.0254*, 2.0256*
Warabi, H. -2.0289
Ward, D.C. -3.0011
Ward, R. -2.0275
Warfield, D.K. -9.0008*
Warren, B.A. -11.0028*
Warren, D.W. -5.0044*, 7.0031*
Waters, J.F. -2.0182, 3.0121, 3.0139
Waterstrat, R.M. -9.0019, 9.0062*
Watkins, F.S. -15.0030*
Watson, E.L. -1.0142*, 2.0057*, 3.0109*
Wawner, F.E. -9.0012*
Weatherall, C. -3.0121
Weatherall, C.C. -3.0139
Weatherell, J.A. -1.0074, 1.0191
Weathers, D.R. -15.0019
Webb, J.G. -8.0002*
Webber, R.L. -1.0179, 1.0187*, 1.0188*, 2.0269*, 2.0270*, 4.0078*
Weber, D.F. -1.0028
Weddup, J. -1.0263*
Wedgwood, D. -9.0100
Wee, E.L. -5.0025
Weedon, L. -2.0129
Wefel, J.S. -1.0251*, 1.0254
Wefel, J.W. -1.0150
Wege, W.R. -11.0023
Wei, S.H. -1.0251
Wei, T.S. -5.0034
Weiffenbach, J.M. -1.0232, 3.0112, 4.0070*, 4.0071, 4.0072, 5.0052
Weigel, R. -3.0132
Weinberg, B. -5.0033
Weinblatt, A. -2.0135, 3.0010
Weiner, R.S. -3.0031
Weinstein, A.M. -9.0083, 9.0084
Weinstein, P. -10.0067*, 13.0007
Weinstein, R. -1.0174
Weinstein, S. -7.0010*
Weinstock, A. -1.0029*
Weiss, M.B. -9.0073*
Weiss, R.E. -2.0228, 4.0022
Wells, J.E. -15.0024
Welten, V. -15.0010
West, D.R. -3.0040
West, E.E. -7.0038
West, N.M. -2.0282, 9.0119
Westerman, R.E. -9.0080*
Weston, J.A. -4.0009*
Westrum, L.E. -10.0017*
Wetherell, J.R. -2.0054*
Whanger, P.D. -1.0039*
Whatley, W.J. -9.0086
Wheatcroft, M.G. -2.0242
Wheeler, L.A. -3.0051*
Wheeler, R.L. -9.0056
Wheeler, T.T. -2.0036
Whitaker, L.A. -6.0012*
White, B. -4.0030, 5.0038
White, C. -3.0035
White, G.C. -2.0089*
White, G.E. -1.0185*
White, S.C. -3.0135*, 11.0022*
Whitford, G.M. -1.0198*, 1.0275*
Whitsel, B.L. -4.0068, 10.0004*, 10.0005*, 10.0006*
Whitson, M. -2.0218
Whitson, S.W. -2.0218*
Whittaker, D.K. -1.0059*
Wible, L.O. -11.0017*
Wick, G. -2.0159*
Wicken, A.J. -1.0114, 1.0115*
Wickstrom, J. -9.0084
Wickwire, N.A. -7.0055
Wiebe, J.D. -1.0187, 2.0269
Wilczek, J. -2.0177, 3.0086
Wilk, A.L. -5.0021
Wilkes, C.M. -2.0178
Wilkinson, G. -3.0040, 3.0113
Willett, N. -1.0110
Williams, B.L. -2.0009, 2.0010*, 2.0028
Williams, C.E. -3.0125
Williams, D.F. -11.0013*
Williams, D.L. -1.0223*, 11.0005*
Williams, J.A. -3.0109
Williams, J.E. -13.0001
Williams, M.L. -9.0104
Williams, R. -2.0193, 4.0047
Williams, S.D. -3.0100*
Wills, D.J. -2.0081
Wilson, C.E. -9.0039
Wilson, J.J. -1.0178
Wilson Mackby, L.F. -5.0036*
Winchell, P.G. -9.0016
Wind, M. -4.0030, 5.0038
Winter, C. -2.0146
Winter, G.B. -14.0003*
Wirthlin, M.R. -2.0187*, 14.0001*, 16.0002
Wise, T. -3.0057
Witkop, C.J. -6.0007
Wittemann, J. -15.0020
Wittemann, J.K. -16.0001*
Wittenberger, C.L. -1.0099*
Wittig, A.B. -1.0282
Witzenberger, T. -2.0274*
Wolf, A.C. -1.0099
Wolf, R.O. -1.0232*, 3.0112, 3.0140*, 4.0071, 4.0072*, 5.0052
Wolpoff, M.H. -12.0002*
Wolskee, P.J. -10.0050
Wondrack, L. -1.0109
Wong, P.Y. -2.0219*, 2.0227*
Wood, R. -15.0027
Woodhouse, R.D. -10.0080
Woodson, K. -2.0228, 4.0022
Woolfson, M. -9.0079
Worms, F.W. -7.0021*
Worrell, D.F. -3.0139
Worthington, B.S. -1.0139*
Wozniak, W.T. -9.0059*
Wright, T.E. -2.0115
Wright, W.E. -2.0026, 2.0271*, 3.0140
Wurster, C. -10.0067
Wuyuan, C. -1.0111
Wyatt, J.R. -3.0101, 11.0017
Wyckoff, R.W. -2.0170*
Wyler, D. -2.0126
Wynder, E.L. -3.0050*
Yaar, M.H. -2.0176, 3.0085, 4.0020, 7.0005
Yaeger, J.A. -7.0056
Yaffe, S.J. -6.0003
Yagi, Y. -1.0208
Yajima, T. -2.0237
Yamada, Y. -7.0053
Yanagisawa, T. -1.0048, 2.0077, 4.0097
Yankell, S.L. -1.0205*, 1.0215
Yeager, J.E. -2.0187, 9.0074*
Yee, J.A. -2.0292*, 4.0013
Yip, W.K. -3.0103
Yokota, T. -10.0032
Yonese, M. -1.0069
Yoon, J. -3.0006, 3.0122
Yoshioka, H. -4.0092
Yotis, W.W. -1.0125*
Youmans, P.A. -1.0047, 1.0048, 1.0049, 1.0051, 1.0052, 2.0077, 2.0182, 2.0228, 3.0139, 4.0022, 4.0097
Young, F.A. -9.0078*, 9.0082
Young, M. -10.0006
Young, R.A. -1.0026*, 1.0036
Young, R.F. -10.0018*, 10.0021*
Zahn, L. -1.0014
Zaki, H.S. -15.0028
Zander, H.A. -2.0263*
Zeeberg, B. -2.0246
Zegarelli, D.J. -15.0021
Zegarelli, E.V. -15.0021
Zeichner, M. -4.0003
Zelson, P. -2.0278*
Zelson, P.R. -2.0279*
Zern, L.D. -1.0178, 1.0179
Ziller, C. -4.0008
Zimmerman, E.F. -4.0033*, 5.0022*, 5.0025*

*INDICATES PRINCIPAL INVESTIGATOR

INVESTIGATOR INDEX

Zingeser, M.R. -6.0002
Zinner, D.D. -1.0219
Zins, J. -6.0012
Zipper, H. -4.0098
Ziriax, J.M. -10.0034
Zlotolow, I. -15.0012
Zoltick, P.W. -5.0034
Zullo, T. -7.0051.

PERFORMING INSTITUTION INDEX

Abcor Inc., Wilmington, Massachusetts
1.0223, 10.0055, 11.0005.
Albert Einstein Medical Center, Philadelphia, Pennsylvania
3.0020.
American Assn. for Dental Research, Washington, District of Columbia
2.0144.
American Cleft Palate Assn., Chapel Hill, North Carolina
5.0036.
American Dental Assn., Chicago, Illinois
1.0041, 1.0067, 1.0070, 1.0227, 2.0290, 6.0005, 7.0041, 9.0019, 9.0021, 9.0023, 9.0059, 9.0062, 9.0064, 9.0103, 10.0056.
American Health Foundation Inc., New York, New York
3.0050.
American Type Culture Collection, Rockville, Maryland
1.0003.
Ankara Oncology Hospital, Ankara, Turkey
3.0070.
Applied Management Sciences Inc., Silver Spring, Maryland
1.0244.
Arignar Anna Memorial Cancer Inst., Kanchipuram, India
3.0042.
Arizona State University, Tempe, Arizona
12.0004.
Battelle Memorial Inst., Columbus, Ohio
9.0038, 9.0072, 11.0012.
Battelle Memorial Inst., Richland, Washington
9.0080.
Baylor College of Dentistry, Dallas, Texas
1.0005.
Baylor College of Medicine, Houston, Texas
1.0103, 3.0023.
Beth Israel Hospital, Boston, Massachusetts
3.0012.
Boston Biomedical Research Inst., Boston, Massachusetts
5.0026.
Boston University, Boston, Massachusetts
3.0133, 15.0029.
Cancer Research Inst., Bombay, India
3.0041, 3.0072, 3.0105.
Case Western Reserve University, Cleveland, Ohio
1.0027, 1.0091, 2.0018, 2.0066, 2.0206, 3.0106, 4.0053, 10.0064.
Childrens Hospital Medical Center, Boston, Massachusetts
2.0189, 2.0222.
Childrens Hospital Medical Center, Cincinnati, Ohio
4.0033, 5.0022, 5.0025.
Childrens Hospital of Philadelphia, Philadelphia, Pennsylvania
5.0027, 6.0003.
Clemson University, Clemson, South Carolina
9.0075, 9.0086, 9.0108.
College of Medicine & Dentistry of New Jersey, Newark, New Jersey
1.0172, 2.0112, 2.0268, 9.0025, 10.0070.
Columbia University, New York, New York
1.0019, 1.0020, 1.0076, 1.0152, 1.0311, 2.0229, 4.0043, 15.0021.
Cooper Lab. Inc., Cedar Knolls, New Jersey
1.0310.
Cornell College, Mount Vernon, Iowa
1.0250, 1.0253.
Cornell University, Ithaca, New York
4.0047.
Creighton University, Omaha, Nebraska
3.0083.
Dental Foundation of North Carolina, Chapel Hill, North Carolina
13.0012.
Duke University, Durham, North Carolina
2.0091, 3.0009, 3.0115, 4.0048, 7.0011.
Dynapol, Palo Alto, California
1.0192.
Eastern Virginia Medical School, Norfolk, Virginia
1.0042.
Eastman Dental Center, Rochester, New York
1.0014, 1.0038, 1.0061, 1.0229, 1.0243, 1.0246, 1.0289, 1.0317, 2.0263, 7.0035, 9.0040.
Emory University, Atlanta, Georgia
3.0029, 3.0132, 5.0003, 9.0008, 15.0019.
Fairleigh Dickinson University, Teaneck, New Jersey
1.0199, 2.0084, 3.0030, 5.0016.
Forsyth Dental Center, Boston, Massachusetts
1.0013, 1.0037, 1.0043, 1.0064, 1.0077, 1.0096, 1.0104, 1.0106, 1.0143, 1.0196, 1.0249, 1.0256, 1.0297, 1.0316, 2.0006, 2.0007, 2.0008, 2.0012, 2.0016, 2.0048, 2.0049, 2.0053, 2.0054, 2.0101, 2.0106, 2.0201, 2.0265, 4.0036, 7.0017.
Franklin Inst. of the State of Pennsylvania, Philadelphia, Pennsylvania
9.0045.
Fred Hutchinson Cancer Research Center, Seattle, Washington
3.0038.
Freie Universitat Berlin, Berlin, Federal Republic of Germany
1.0054, 9.0044.
Geauga County General Health District, Chardon, Ohio
1.0327.
George Washington University, Washington, District of Columbia
9.0047.
Georgetown University, Washington, District of Columbia
1.0080, 3.0145, 4.0015, 5.0017.
Georgia Inst. of Technology, Atlanta, Georgia
1.0026, 1.0036, 9.0009.
Glasgow Dental Hospital & School, Glasgow, Scotland, United Kingdom
2.0035, 2.0047.
Goteborgs Universitet, Goteborg, Sweden
2.0267.
Grupo de Estudio sobre Occlusion F A C T A, Mexico City, Mexico
4.0093.
Gujarat Cancer & Research Inst., Ahmedabad, India
3.0047.
Hahnemann Medical College & Hospital, Philadelphia, Pennsylvania
3.0087.
Harvard University, Boston, Massachusetts
1.0328, 1.0329, 2.0114, 2.0150, 2.0193, 2.0215, 2.0226, 3.0011, 3.0032, 3.0080, 4.0042, 5.0014, 5.0015, 8.0001, 9.0079, 9.0085, 15.0031.
Haskins Lab. Inc., New Haven, Connecticut
4.0092.
Hazleton Lab. America Inc., Vienna, Virginia
1.0176, 1.0293.
Hospital for Special Surgery, New York, New York

PERFORMING INSTITUTION INDEX

1.0177.

Howard University, Washington, District of Columbia
1.0060, 1.0165, 2.0065, 2.0188, 7.0008, 11.0030.

Independence Neighborhood Council, Independence, Missouri
1.0322.

Indiana University, Indianapolis, Indiana
1.0255, 2.0003, 2.0248, 5.0002, 5.0033, 9.0016.

Indianapolis Center for Advanced Research Inc., Indianapolis, Indiana
9.0106.

Inst. de Seguridad Social, Medellin, Colombia
3.0073.

Inst. for Medical Research, Kuala Lumpur, Malaysia
3.0043.

Inst. for Medical Research of Bennington, Bennington, Vermont
6.0004.

Inst. of Dental Research, Sydney, Australia
1.0114.

Institut Gustave Roussy, Paris, France
3.0064.

International Assn. for Dental Research, Chicago, Illinois
10.0087.

International Assn. for the Study of Pain, Washington, District of Columbia
10.0001.

Iowa State University of Science & Technology, Ames, Iowa
2.0043.

Istituto di Oncologia, Torino, Italy
3.0060.

Johns Hopkins University, Baltimore, Maryland
5.0023, 5.0034, 6.0006.

Katholieke Universiteit Nijmegen, Nijmegen, Netherlands
9.0111, 15.0010.

Kent State University, Kent, Ohio
10.0066.

Kobenhavns Tandlaegehojskole, Copenhagen, Denmark
3.0063, 3.0092.

Lake Pontchartrain Lab., New Orleans, Louisiana
9.0050.

Lancaster Cleft Palate Clinic, Lancaster, Pennsylvania
5.0037, 10.0073.

Leopold Franzens Universitat Innsbruck, Innsbruck, Austria
2.0159, 7.0029.

Litton Bionetics Inc., Kensington, Maryland
3.0003.

Los Angeles County Harbor General Hospital, Torrance, California
10.0018.

Louisiana State University, New Orleans, Louisiana
1.0230, 9.0020.

Loyola University of Chicago, Hines, Illinois
1.0125.

Loyola University of Chicago, Maywood, Illinois
2.0064, 2.0204, 3.0054, 4.0037.

Marquette University, Milwaukee, Wisconsin
5.0029, 9.0063.

Massachusetts General Hospital, Boston, Massachusetts
4.0006, 4.0017, 10.0078.

Mayo Foundation, Rochester, Minnesota
3.0024, 10.0084.

McGill University, Montreal, Quebec, Canada
1.0044.

Medical College Hospitals, Calcutta, India
3.0102.

Medical College of Georgia, Augusta, Georgia
1.0033, 1.0198, 1.0275, 2.0037, 3.0019, 3.0137, 3.0147, 3.0153, 4.0088, 7.0046, 9.0015, 9.0017, 9.0058, 10.0027, 11.0023.

Medical College of Pennsylvania, Philadelphia, Pennsylvania
1.0300.

Medical Research Council, Bristol, England, United Kingdom
1.0055, 1.0086, 2.0259, 4.0049.

Medical Research Council, London, England, United Kingdom
1.0012.

Medical Research Foundation of Oregon, Portland, Oregon
6.0002.

Medical University of South Carolina, Charleston, South Carolina
2.0075, 9.0078, 9.0082.

Meharry Medical College, Nashville, Tennessee
7.0019.

Memorial Hospital for Cancer & Allied Diseases, New York, New York
15.0025.

Michigan State University, East Lansing, Michigan
1.0210, 5.0012.

Microbiological Associates Inc., Bethesda, Maryland
2.0060.

Ministry of Health & Social Services, Hamilton, Bermuda
1.0263.

Monell Chemical Senses Center, Philadelphia, Pennsylvania
7.0026, 10.0026, 10.0041.

Nassau County Medical Center, East Meadow, New York
9.0118.

National Bank of Egypt, Cairo, Egypt
7.0014.

National Cancer Registry, Colombo, Sri Lanka
3.0069.

National Defense Medical Center, Taipei, Republic of China
1.0169.

National University of Ireland, Cork, Ireland
9.0113.

National University of Ireland, Dublin, Ireland
3.0067.

National University of Mexico, Mexico City, Mexico
13.0009.

New Jersey Inst. of Technology, Newark, New Jersey
9.0039.

New York Medical College, New York, New York
1.0068, 3.0053.

New York Medical College, Valhalla, New York
2.0227.

New York University, New York, New York
1.0035, 1.0071, 3.0015, 4.0028, 4.0075, 4.0079, 4.0080, 9.0029.

North Dakota State University, Fargo, North Dakota
10.0068.

Northern California Cancer Program Inc., Palo Alto, California
3.0094, 15.0011.

Northwestern University, Chicago, Illinois
1.0109, 1.0111, 1.0126, 2.0164, 2.0172, 3.0096, 5.0001, 9.0010, 9.0024, 9.0026, 9.0028, 9.0056.

Northwestern University, Evanston, Illinois
10.0020.

Ohio State University, Columbus, Ohio
1.0053, 1.0094.

Oregon State Higher Education System, Corvallis, Oregon
1.0039.

Oregon State Higher Education System, Eugene, Oregon
4.0009.

Oregon State Higher Education System, Portland, Oregon
1.0031, 1.0040, 1.0240, 1.0288, 2.0143, 2.0262, 9.0005, 9.0006, 10.0013, 10.0082.

Pan American Health & Education Foundation, Washington, District of Columbia
1.0001.

Pennsylvania State University, University Park, Pennsylvania
2.0202, 2.0208.

PLAPO, Santiago, Chile
3.0048.

Polymer Corp. of America, Brooklyn, New York
9.0037.

Queens University of Belfast, Belfast, Northern Ireland, United Kingdom
3.0071.

Rensselaer Polytechnic Inst., Troy, New York
9.0087.

Research for Health in Erie County Inc., Buffalo, New York
1.0326.

Rijksuniversiteit te Gent, Ghent, Belgium
15.0003.

Rijksuniversiteit te Utrecht, Utrecht, Netherlands
1.0023, 4.0058.

Royal College of Surgeons of England, London, England, United Kingdom
1.0136, 1.0292, 1.0308, 2.0137.

PERFORMING INSTITUTION INDEX

Royal Dental College, Copenhagen, Denmark
3.0075, 3.0093.
Rush Presbyterian St. Lukes Medical Center, Chicago, Illinois
9.0073.
Rutgers the State University of New Jersey, New Brunswick, New Jersey
2.0250.
S R I International, Menlo Park, California
1.0193.
Semmelweis Orvostudomanyi Egyetem, Budapest, Hungary
1.0195, 3.0074.
Solid Photography Inc., Melville, New York
9.0054.
Southern Illinois University, Edwardsville, Illinois
2.0218, 3.0146, 11.0037.
Southern Research Inst., Birmingham, Alabama
1.0241, 9.0046, 9.0060, 9.0071.
Southwest Research Inst., San Antonio, Texas
9.0107.
St. Francis Xavier Hospital, Charleston, South Carolina
5.0051.
St. Jude Childrens Research Hospital, Memphis, Tennessee
1.0146.
Stanford University, Stanford, California
11.0002.
State Dept. of Health, Denver, Colorado
1.0325.
State Dept. of Health & Environmental Sciences, Helena, Montana
1.0320.
State Dept. of Health & Social Services, Madison, Wisconsin
12.0001.
State Dept. of Public Health, Lansing, Michigan
1.0319.
State University of New York, Buffalo, New York
1.0002, 1.0065, 1.0092, 1.0120, 1.0123, 1.0231, 1.0294, 1.0296, 2.0013, 2.0061, 2.0102, 2.0104, 2.0105, 2.0117, 2.0121, 2.0140, 2.0154, 2.0221, 2.0247, 2.0266, 3.0017, 3.0039, 3.0040, 3.0118, 3.0155, 7.0001, 7.0034, 7.0057, 9.0081, 9.0115, 10.0065, 10.0086, 11.0021, 15.0023.
State University of New York, Stony Brook, New York
1.0144, 1.0148, 1.0153, 1.0247, 1.0315, 2.0107, 2.0168, 4.0011, 9.0022.
State University of New York, Syracuse, New York
10.0040.
State University System of Florida, Gainesville, Florida
1.0004, 1.0034, 1.0134, 1.0207, 2.0036, 2.0050, 2.0113, 2.0119, 4.0064, 7.0023, 7.0025, 7.0055, 7.0058, 9.0088.
State University System of Florida, Tampa, Florida
3.0022, 5.0030.
Stevens Inst. of Technology, Hoboken, New Jersey
1.0121, 1.0154.
Strangeways Research Lab., Cambridge, England, United Kingdom
4.0060.
Tata Inst. of Fundamental Research, Bombay, India
3.0049, 3.0065, 3.0066, 3.0104.
Temple University, Philadelphia, Pennsylvania
1.0110, 1.0173, 1.0174, 3.0107, 3.0116, 10.0063, 10.0069, 15.0022.
Texas A & M University, College Station, Texas
4.0046.
Texas Tech University, Lubbock, Texas
2.0292, 4.0013.
Tufts University, Boston, Massachusetts
1.0185, 1.0301, 6.0013, 7.0040, 15.0026.
Tulane University of Louisiana, New Orleans, Louisiana
9.0083, 9.0084.
U.S. Dept. of Commerce
..National Bureau of Standards, Washington, District of Columbia
1.0045, 9.0041.
U.S. Dept. of Defense
..Army
....Medical Research & Development Command
......Div. of Basic Sciences, Washington, District of Columbia
2.0184, 2.0260, 9.0114, 11.0006, 11.0033.
......Div. of Dental Materials, Washington, District of Columbia
9.0001, 9.0055, 10.0083, 11.0007, 11.0034.
......Div. of Pathology, Washington, District of Columbia
3.0001, 11.0014.
......Div. of Surgery, Washington, District of Columbia
8.0003, 9.0101.
......Inst. of Dental Research, Washington, District of Columbia
2.0123, 3.0159, 8.0002, 11.0008, 11.0009, 11.0010, 11.0011.
......Preventive Dentistry Div., Washington, District of Columbia
15.0008.
..Defense Nuclear Agency
....Armed Forces Radiobiology Research Inst., Bethesda, Maryland
8.0004.
..Navy
....Naval Dental Research Inst., Great Lakes, Illinois
1.0239, 11.0001.
......Biochemistry Div., Great Lakes, Illinois
1.0137.
......Clinical Investigation Dept., Great Lakes, Illinois
2.0187, 3.0160, 9.0074, 14.0001, 16.0002.
......Histopathology Div., Great Lakes, Illinois
2.0186.
......Microbiology Div., Great Lakes, Illinois
1.0204, 1.0222.
....Naval Graduate Dental School
......National Naval Dental Center, Bethesda, Maryland
13.0001.
....Naval Medical Research Inst.
......Clinical Sciences Div., Bethesda, Maryland
2.0185, 8.0005.
......Dental Sciences Dept., Bethesda, Maryland
3.0161.
U.S. Dept. of Health & Human Services, San Francisco, California
1.0330.
..Public Health Service
....Hospital, San Francisco, California
9.0030.
....National Inst. of Health
......National Heart Lung & Blood Inst., Bethesda, Maryland
5.0021.
......National Inst. of Dental Research, Bethesda, Maryland
1.0008, 1.0009, 1.0010, 1.0011, 1.0022, 1.0046, 1.0047, 1.0048, 1.0049, 1.0050, 1.0051, 1.0052, 1.0084, 1.0085, 1.0099, 1.0100, 1.0101, 1.0102, 1.0128, 1.0129, 1.0130, 1.0131, 1.0132, 1.0133, 1.0155, 1.0156, 1.0157, 1.0158, 1.0159, 1.0160, 1.0166, 1.0175, 1.0178, 1.0179, 1.0187, 1.0188, 1.0194, 1.0201, 1.0203, 1.0214, 1.0215, 1.0216, 1.0217, 1.0218, 1.0232, 1.0233, 1.0234, 1.0257, 1.0258, 1.0259, 1.0260, 1.0261, 1.0277, 1.0278, 1.0279, 1.0280, 1.0281, 1.0282, 1.0283, 1.0284, 1.0302, 1.0303, 1.0304, 1.0305, 2.0024, 2.0025, 2.0026, 2.0027, 2.0028, 2.0051, 2.0076, 2.0077, 2.0078, 2.0079, 2.0080, 2.0124, 2.0125, 2.0126, 2.0127, 2.0128, 2.0129, 2.0130, 2.0131, 2.0132, 2.0133, 2.0134, 2.0135, 2.0145, 2.0146, 2.0176, 2.0177, 2.0178, 2.0182, 2.0228, 2.0239, 2.0240, 2.0269, 2.0270, 2.0271, 2.0284, 2.0289, 3.0005, 3.0006, 3.0007, 3.0010, 3.0037, 3.0057, 3.0085, 3.0086, 3.0121, 3.0122, 3.0123, 3.0139, 3.0140, 4.0020, 4.0021, 4.0022, 4.0023, 4.0024, 4.0030, 4.0045, 4.0054, 4.0070, 4.0071, 4.0072, 4.0078, 4.0097, 5.0019, 5.0031, 5.0038, 5.0052, 7.0005, 7.0042, 7.0049, 10.0030, 10.0031, 10.0032, 10.0033, 10.0034, 10.0035, 10.0036, 10.0037, 10.0038, 10.0049, 10.0050, 10.0051, 10.0052, 10.0058, 10.0071, 17.0001.
......National Inst. on Aging, Baltimore, Maryland
3.0112.
U.S. Dept. of Health Education & Welfare
..Public Health Service
....Health Services Admin.
......Indian Health Service, Shiprock, New Mexico
7.0048.
U.S. Veterans Admin.
..Dept. of Medicine & Surgery
....Medical Center, Loma Linda, California
2.0062, 3.0141, 9.0095, 11.0015.
Long Beach, California
1.0072, 1.0073, 2.0147, 3.0089, 3.0162, 6.0014.

Los Angeles, California
2.0030, 2.0031, 2.0032, 2.0033, 2.0157, 2.0183, 2.0280, 2.0287, 3.0150, 5.0039, 9.0031, 9.0069, 10.0081, 11.0016, 11.0026.
Palo Alto, California
3.0151, 10.0079.
San Diego, California
2.0029.
Sepulveda, California
4.0062, 9.0066, 9.0089.
Denver, Colorado
2.0232, 3.0114.
West Haven, Connecticut
11.0003, 11.0025, 13.0004.
Wilmington, Delaware
9.0051.
Washington, District of Columbia
2.0233, 3.0124.
Bay Pines, Florida
1.0219.
Gainesville, Florida
3.0031.
Miami, Florida
1.0161, 1.0162, 1.0312.
Chicago, Illinois
9.0090.
Indianapolis, Indiana
2.0274, 3.0100, 9.0092, 9.0093.
Marion, Indiana
11.0018.
Iowa City, Iowa
1.0235.
Knoxville, Iowa
10.0080.
Leavenworth, Kansas
2.0136, 2.0156, 2.0234, 2.0235, 2.0253, 2.0254, 2.0256, 9.0033, 11.0027.
Lexington, Kentucky
2.0231.
Togus, Maine
3.0059, 11.0004.
Perry Point, Maryland
2.0283.
Bedford, Massachusetts
1.0224.
West Roxbury, Massachusetts
2.0272, 4.0055, 4.0099, 9.0094, 11.0029.
Allen Park, Michigan
9.0068.
Ann Arbor, Michigan
2.0155, 2.0252, 3.0142, 4.0031, 7.0027, 7.0052, 9.0122.
Battle Creek, Michigan
1.0313.
Columbia, Missouri
9.0096.
East Orange, New Jersey
3.0099.
Brooklyn, New York
2.0273, 4.0098, 10.0054, 10.0060.
Buffalo, New York
2.0093, 3.0088, 3.0113.
New York, New York
2.0241, 2.0275, 9.0091.
Asheville, North Carolina
3.0148.
Durham, North Carolina
11.0031.
Dayton, Ohio
15.0004.
Oklahoma City, Oklahoma
2.0055, 10.0059.
Roseburg, Oregon
15.0009.
Philadelphia, Pennsylvania
2.0278, 2.0279, 10.0043.
Memphis, Tennessee
3.0101, 11.0017.
Dallas, Texas
9.0097, 9.0098.
Houston, Texas
1.0262, 3.0149.
San Antonio, Texas
9.0032.
Temple, Texas
9.0070.
Hampton, Virginia
3.0058, 7.0059.
Richmond, Virginia
2.0282, 3.0158, 9.0119.
Vancouver, Washington
9.0042.
Martinsburg, West Virginia
2.0277, 3.0143.
Wood, Wisconsin
2.0276, 9.0067.
....Outpatient Clinic, Boston, Massachusetts
2.0002, 2.0230, 2.0281, 11.0019.
Universidad de Buenos Aires, Buenos Aires, Argentina
9.0043.
Universidad Nacional de Cordoba, Cordoba, Argentina
2.0288, 3.0061, 3.0126, 3.0127, 3.0128, 3.0156, 4.0056, 4.0057, 4.0061, 9.0034, 9.0035, 9.0036, 9.0112, 9.0123.
Universitat Klinik fur Zahn Mund und Kieferheilkunde, Graz, Austria
1.0236.
Universite dAix Marseille, Marseille, France
1.0170, 1.0190, 1.0237, 2.0149, 4.0050, 6.0009, 10.0046, 11.0020.
Universite de Nantes, Nantes, France
4.0008.
Universitet i Bergen, Bergen, Norway
2.0017.
University Hospital, Copenhagen, Denmark
3.0062.
University of Adelaide, Adelaide, Australia
1.0016, 12.0005.
University of Alabama in Birmingham, Birmingham, Alabama
1.0062, 1.0063, 1.0078, 1.0108, 1.0138, 1.0149, 1.0163, 1.0164, 1.0197, 1.0206, 1.0228, 1.0291, 1.0318, 2.0058, 2.0059, 2.0073, 2.0098, 2.0099, 2.0162, 2.0163, 2.0181, 2.0200, 3.0021, 3.0111, 3.0131, 4.0065, 9.0049, 9.0053, 15.0013.
University of Alberta, Edmonton, Alberta, Canada
7.0007.
University of Arizona, Tucson, Arizona
2.0170, 5.0050.
University of Baghdad, Baghdad, Iraq
3.0090.
University of Birmingham, Birmingham, England, United Kingdom
1.0168, 14.0002.
University of Bristol, Bristol, England, United Kingdom
1.0220, 2.0082, 2.0083, 10.0044.
University of British Columbia, Vancouver, British Columbia, Canada
1.0167, 5.0032.
University of California, Berkeley, California
1.0066.
University of California, Los Angeles, California
1.0029, 2.0044, 2.0203, 3.0051, 3.0135, 4.0089, 5.0035, 9.0121, 10.0012, 10.0028, 11.0022, 13.0006, 15.0018.
University of California, San Francisco, California
1.0075, 1.0323, 2.0175, 3.0025, 3.0035, 4.0076, 4.0091, 7.0009, 7.0013, 7.0037, 7.0038, 10.0023, 11.0024, 15.0012.
University of California, Torrance, California
10.0021.
University of Chicago, Chicago, Illinois
1.0295, 1.0299, 3.0097, 4.0066, 7.0012.
University of Colorado, Denver, Colorado
1.0082, 2.0022, 2.0046, 3.0154, 15.0027.
University of Connecticut, Farmington, Connecticut
1.0021, 1.0171, 1.0184, 1.0200, 1.0221, 1.0238, 1.0290, 1.0298, 1.0314, 2.0005, 2.0038, 2.0092, 2.0165, 2.0179, 2.0211, 2.0212, 3.0052, 4.0025, 4.0026, 4.0094, 7.0010,

PERFORMING INSTITUTION INDEX

7.0020, 7.0039, 7.0050, 7.0056, 9.0116, 10.0048, 10.0072, 13.0005, 13.0011.

University of Connecticut, Storrs, Connecticut
2.0023, 2.0207, 4.0082, 9.0027.

University of Denver, Denver, Colorado
2.0042.

University of Durban Westville, Durban, South Africa
3.0068, 3.0091.

University of Glasgow, Glasgow, Scotland, United Kingdom
1.0087.

University of Illinois, Chicago, Illinois
1.0028, 1.0145, 1.0151, 2.0001, 3.0081, 4.0001, 4.0002, 4.0027, 4.0074, 4.0087, 5.0006, 5.0007, 5.0008, 5.0042, 5.0045, 6.0001, 6.0010, 6.0011, 7.0015, 7.0016, 7.0022, 7.0030, 7.0033, 10.0024, 10.0077.

University of Illinois, Urbana, Illinois
9.0110.

University of Iowa, Iowa City, Iowa
1.0150, 1.0202, 1.0251, 1.0254, 3.0028, 3.0084, 4.0084, 5.0004, 5.0040, 5.0041, 5.0047, 10.0014, 10.0039.

University of Kansas, Kansas City, Kansas
2.0214, 3.0138, 4.0044.

University of Kentucky, Lexington, Kentucky
2.0052, 2.0217, 15.0005, 15.0016, 16.0004.

University of Leeds, Leeds, England, United Kingdom
1.0056, 1.0057, 1.0074, 1.0191.

University of Liverpool, Liverpool, England, United Kingdom
1.0088, 11.0013.

University of London, London, England, United Kingdom
1.0017, 1.0058, 1.0189, 1.0225, 1.0307, 2.0034, 2.0063, 2.0081, 2.0138, 2.0148, 2.0236, 3.0033, 3.0045, 3.0046, 3.0103, 5.0020, 7.0018, 7.0028, 9.0052, 10.0045, 10.0047, 13.0013, 14.0003.

University of Louisville, Louisville, Kentucky
1.0098, 1.0212, 15.0017.

University of Maine, Orono, Maine
4.0018.

University of Manchester, Manchester, England, United Kingdom
1.0135, 1.0264, 4.0059, 9.0099.

University of Manitoba, Winnipeg, Manitoba, Canada
9.0100.

University of Maryland, Baltimore, Maryland
1.0083, 1.0112, 2.0120, 2.0171, 3.0120, 9.0011, 15.0001.

University of Maryland, College Park, Maryland
5.0043.

University of Massachusetts, Amherst, Massachusetts
2.0021.

University of Massachusetts, Worcester, Massachusetts
2.0205, 2.0216.

University of Miami, Coral Gables, Florida
1.0093, 1.0095, 1.0118, 1.0147, 1.0213.

University of Michigan, Ann Arbor, Michigan
1.0025, 1.0030, 1.0069, 1.0079, 1.0119, 1.0186, 1.0208, 1.0209, 1.0248, 2.0074, 2.0100, 2.0139, 2.0153, 2.0264, 2.0286, 3.0013, 3.0014, 3.0036, 4.0010, 4.0039, 4.0040, 4.0041, 4.0067, 4.0073, 4.0090, 5.0009, 5.0011, 7.0002, 7.0006, 7.0024, 7.0043, 7.0047, 7.0053, 9.0007, 9.0014, 9.0048, 9.0061, 10.0074, 12.0002.

University of Minnesota, Minneapolis, Minnesota
1.0024, 1.0032, 1.0097, 1.0127, 1.0181, 1.0265, 1.0266, 1.0267, 1.0268, 1.0269, 1.0270, 1.0271, 1.0272, 1.0273, 1.0286, 2.0039, 2.0180, 2.0190, 2.0191, 2.0192, 2.0249, 3.0082, 3.0157, 6.0007, 7.0021.

University of Mississippi, Jackson, Mississippi
1.0122, 3.0016.

University of Missouri, Columbia, Missouri
2.0220.

University of Missouri, Kansas City, Missouri
2.0258.

University of Missouri, Rolla, Missouri
1.0226.

University of Nebraska, Lincoln, Nebraska
15.0007.

University of New Mexico, Albuquerque, New Mexico
3.0095.

University of New South Wales, Kensington, Australia
1.0115.

University of North Carolina, Chapel Hill, North Carolina
1.0182, 1.0183, 1.0274, 1.0276, 1.0287, 2.0071, 2.0072, 2.0089, 2.0152, 2.0160, 2.0161, 2.0173, 2.0195, 2.0196, 2.0197, 2.0198, 2.0199, 2.0244, 2.0245, 2.0246, 2.0291, 3.0129, 3.0130, 3.0136, 4.0012, 4.0034, 4.0052, 4.0063, 4.0068, 4.0085, 4.0095, 5.0010, 5.0044, 7.0031, 7.0032, 7.0036, 7.0045, 9.0002, 9.0003, 9.0004, 9.0057, 9.0065, 9.0076, 9.0077, 9.0102, 10.0004, 10.0005, 10.0006, 10.0007, 10.0008, 10.0085, 13.0008, 15.0002, 15.0015.

University of Oklahoma, Oklahoma City, Oklahoma
1.0306, 9.0120, 15.0030.

University of Pennsylvania, Philadelphia, Pennsylvania
1.0015, 1.0107, 1.0205, 1.0252, 2.0011, 2.0015, 2.0019, 2.0045, 2.0068, 2.0069, 2.0070, 2.0088, 2.0096, 2.0097, 2.0108, 2.0116, 2.0257, 2.0285, 3.0004, 3.0056, 3.0110, 3.0119, 5.0028, 6.0012, 7.0003, 9.0117, 11.0035, 11.0036, 13.0002.

University of Pittsburgh, Pittsburgh, Pennsylvania
1.0117, 1.0124, 3.0008, 4.0051, 4.0077, 4.0086, 5.0046, 5.0048, 5.0049, 7.0051, 9.0104, 15.0028.

University of Pretoria, Pretoria, South Africa
3.0076.

University of Puerto Rico, Rio Piedras, Puerto Rico
7.0004.

University of Queensland, Brisbane, Australia
4.0032.

University of Rochester, Rochester, New York
1.0113, 2.0251.

University of Sheffield, Sheffield, England, United Kingdom
2.0158.

University of Southern California, Los Angeles, California
2.0118, 2.0167, 2.0213, 3.0108, 4.0003, 4.0004, 4.0005, 4.0007, 4.0014, 4.0035, 5.0005, 5.0013, 5.0024, 10.0010.

University of Stellenbosch, Tygerberg, South Africa
1.0089, 1.0090, 1.0309, 3.0044, 3.0077.

University of Tennessee, Memphis, Tennessee
2.0169, 2.0219, 4.0019, 15.0024.

University of Texas, Austin, Texas
4.0016.

University of Texas, Dallas, Texas
7.0044.

University of Texas, Houston, Texas
1.0081, 1.0105, 1.0211, 1.0242, 1.0245, 1.0324, 2.0004, 2.0109, 2.0110, 2.0115, 2.0174, 2.0237, 2.0238, 2.0242, 2.0255, 2.0261, 3.0078, 4.0096, 10.0057.

University of Texas, San Antonio, Texas
1.0285, 9.0109, 10.0042.

University of the Pacific, San Francisco, California
7.0060, 9.0018.

University of the Witwatersrand, Johannesburg, South Africa
3.0125.

University of Toronto, Toronto, Ontario, Canada
1.0006, 9.0124, 10.0015, 10.0025.

University of Virginia, Charlottesville, Virginia
9.0012, 9.0013.

University of Wales, Cardiff, Wales, United Kingdom
1.0059, 2.0085, 3.0034.

University of Washington, Seattle, Washington
1.0139, 1.0140, 1.0141, 1.0142, 2.0009, 2.0010, 2.0056, 2.0057, 2.0067, 2.0086, 2.0087, 2.0094, 2.0095, 2.0142, 2.0151, 2.0166, 2.0194, 2.0243, 3.0026, 3.0027, 3.0055, 3.0109, 3.0144, 3.0152, 4.0029, 4.0038, 4.0081, 6.0008, 7.0054, 9.0105, 10.0002, 10.0003, 10.0009, 10.0016, 10.0017, 10.0019, 10.0053, 10.0061, 10.0067, 10.0076, 13.0003, 13.0007, 13.0010, 15.0006, 16.0003.

University of Western Ontario, London, Ontario, Canada
1.0007, 11.0028, 11.0032.

University of Wisconsin, Madison, Wisconsin
3.0134.

Utah Higher Education System, Salt Lake City, Utah
2.0225, 3.0002.

Virginia Commonwealth University, Richmond, Virginia
1.0116, 1.0180, 1.0321, 2.0014, 2.0020, 2.0090, 2.0103, 2.0111, 2.0122, 3.0018, 3.0098, 4.0069, 15.0020, 16.0001.

Virginia Polytechnic Inst. & State University, Blacksburg, Virginia
2.0040.

Wake Forest University, Winston Salem, North Carolina

10.0022.

Washington State University, Pullman, Washington
2.0224, 10.0029.

Washington University, St. Louis, Missouri
2.0209, 2.0223, 12.0003, 15.0014.

Wayne State University, Detroit, Michigan
3.0117, 10.0075.

West Virginia University, Morgantown, West Virginia
2.0041, 2.0141, 10.0011.

Westat Inc., Rockville, Maryland
1.0018.

Western Washington University, Bellingham, Washington
10.0062.

Wheaton College, Norton, Massachusetts
5.0018.

Wright State University, Dayton, Ohio
4.0083.

Yale University, New Haven, Connecticut
2.0210, 3.0079.

SUPPORTING AGENCY INDEX

American Fund for Dental Health, Chicago, Illinois
6.0005, 13.0005, 13.0006, 13.0007, 13.0008, 15.0001, 15.0002, 16.0001.
Canadian Dept. of National Health & Welfare, Ottawa, Ontario, Canada
7.0007.
Consejo Nacional de Investigaciones Cientificas y Technicas, Buenos Aires, Argentina
9.0043.
Council for Tobacco Research U.S.A. Inc., New York, New York
3.0032.
Dept. of Atomic Energy, Bombay, India
3.0072.
Florida State Government, Tallahassee, Florida
1.0134.
Freie Universitat Berlin, Berlin, Federal Republic of Germany
1.0054, 9.0044.
Government of Netherlands, The Hague, Netherlands
15.0010.
Grupo de Estudio sobre Occlusion F A C T A, Mexico City, Mexico
4.0093.
Gujarat Cancer & Research Inst., Ahmedabad, India
3.0047.
Inst. de Seguridad Social, Medellin, Colombia
3.0073.
Leopold Franzens Universitat Innsbruck, Innsbruck, Austria
7.0029.
Medical Research Council, London, England, United Kingdom
1.0012, 1.0017, 1.0055, 1.0056, 1.0057, 1.0058, 1.0086, 1.0087, 1.0088, 1.0135, 1.0136, 1.0168, 1.0189, 1.0220, 1.0225, 1.0264, 1.0292, 1.0307, 1.0308, 2.0034, 2.0063, 2.0082, 2.0083, 2.0085, 2.0137, 2.0148, 2.0158, 2.0259, 3.0034, 4.0049, 4.0059, 4.0060, 9.0052, 9.0099, 10.0044, 10.0045, 11.0013, 13.0013, 14.0002, 14.0003.
Medical Research Council of Canada, Ottawa, Ontario, Canada
5.0032.
Ministry of Health, Budapest, Hungary
3.0074.
National Geographic Society, Washington, District of Columbia
12.0004.
National Health & Medical Research Council, Canberra, Australia
1.0016.
National Science Council, Taipei, Republic of China
1.0169.
National University of Ireland, Cork, Ireland
9.0113.
New York State Government, Albany, New York
4.0047.
Ohio State University, Columbus, Ohio
1.0053.
Ontario Provincial Government, Toronto, Ontario, Canada
11.0028, 11.0032.
Osterreichischer Fonds zur Forderung wissenschaft. Forschung, A-1090 Vienna, Austria
1.0236.
Rijksuniversiteit te Gent, Ghent, Belgium
15.0003.
Royal Dental College, Copenhagen, Denmark
3.0075, 3.0093.
Scientific Research Council, Hungary
1.0195.
South African Medical Research Council, Tygerberg, South Africa
1.0089, 1.0090, 1.0309, 3.0076, 3.0077.
Southern Illinois University, Edwardsville, Illinois
11.0037.
U.S. Dept. of Defense
..Army
....Medical Research & Development Command
9.0071, 10.0055, 11.0005.
......Care of the Wounded Div.
10.0082.
......Dental Research Div.
9.0072, 9.0073.
......Inst. of Dental Research
1.0221, 1.0226, 1.0310, 2.0184, 2.0260, 3.0001, 3.0159, 8.0002, 8.0003, 9.0001, 9.0037, 9.0053, 9.0054, 9.0055, 9.0101, 9.0114, 10.0083, 11.0006, 11.0007, 11.0008, 11.0009, 11.0010, 11.0011, 11.0014, 11.0033, 11.0034, 15.0008.
......Medical Bioengineering Research & Development Lab.
1.0238, 9.0045, 11.0012.
..Defense Nuclear Agency
....Armed Forces Radiobiology Research Inst.
8.0004.
..Navy
....Naval Medical Research & Development Command
......National Naval Medical Center
1.0137, 1.0204, 1.0222, 1.0239, 2.0185, 2.0186, 2.0187, 3.0160, 3.0161, 8.0005, 9.0074, 11.0001, 13.0001, 14.0001, 16.0002.
....Office of Naval Research
1.0184, 1.0227, 2.0064.
U.S. Dept. of Health & Human Services
..Public Health Service
....Center for Disease Control
......National Inst. for Occupational Safety & Health
10.0056, 11.0002, 11.0035.
....Food & Drug Admin.
11.0021.
......Bureau of Radiological Health
11.0022, 11.0023, 11.0024.
....National Inst. of Health
......Div. of Research Resources
1.0060, 1.0103, 2.0065, 2.0188, 2.0290, 7.0008, 10.0002, 11.0030, 11.0036.
......Fogarty International Center
3.0049, 7.0014.
......National Cancer Inst.
3.0050, 3.0051, 3.0078, 3.0079, 3.0080, 3.0094, 3.0095, 3.0096, 3.0097, 9.0056, 15.0011, 15.0012, 15.0013, 15.0014, 15.0015, 15.0016, 15.0017, 15.0018, 15.0019, 15.0020, 15.0021, 15.0022, 15.0023, 15.0024, 15.0025, 15.0026, 15.0027, 15.0028, 15.0029, 15.0030, 15.0031.
......National Eye Inst.
3.0011.
......National Heart Lung & Blood Inst.
5.0021.
......National Inst. of Allergy & Infectious Diseases
3.0008.
......National Inst. of Arthritis Metabolism & Digestive Diseases
2.0150, 2.0189, 6.0006, 9.0075.
......National Inst. of Child Health & Human Development
4.0033, 5.0022.

SUPPORTING AGENCY INDEX

......National Inst. of Dental Research
1.0001, 1.0002, 1.0003, 1.0004, 1.0005, 1.0006, 1.0007, 1.0008, 1.0009, 1.0010, 1.0011, 1.0013, 1.0014, 1.0015, 1.0018, 1.0019, 1.0020, 1.0021, 1.0022, 1.0024, 1.0025, 1.0026, 1.0027, 1.0028, 1.0029, 1.0030, 1.0031, 1.0032, 1.0033, 1.0034, 1.0035, 1.0036, 1.0037, 1.0038, 1.0039, 1.0040, 1.0041, 1.0042, 1.0043, 1.0044, 1.0045, 1.0046, 1.0047, 1.0048, 1.0049, 1.0050, 1.0051, 1.0052, 1.0061, 1.0062, 1.0063, 1.0064, 1.0065, 1.0066, 1.0067, 1.0068, 1.0069, 1.0070, 1.0071, 1.0075, 1.0076, 1.0077, 1.0078, 1.0079, 1.0080, 1.0081, 1.0082, 1.0083, 1.0084, 1.0085, 1.0091, 1.0092, 1.0093, 1.0094, 1.0095, 1.0096, 1.0097, 1.0098, 1.0099, 1.0100, 1.0101, 1.0102, 1.0104, 1.0105, 1.0106, 1.0107, 1.0108, 1.0109, 1.0110, 1.0111, 1.0112, 1.0113, 1.0114, 1.0115, 1.0116, 1.0117, 1.0118, 1.0119, 1.0120, 1.0121, 1.0122, 1.0123, 1.0124, 1.0125, 1.0126, 1.0127, 1.0128, 1.0129, 1.0130, 1.0131, 1.0132, 1.0133, 1.0138, 1.0139, 1.0140, 1.0141, 1.0142, 1.0143, 1.0144, 1.0145, 1.0146, 1.0147, 1.0148, 1.0149, 1.0150, 1.0151, 1.0152, 1.0153, 1.0154, 1.0155, 1.0156, 1.0157, 1.0158, 1.0159, 1.0160, 1.0163, 1.0164, 1.0165, 1.0166, 1.0171, 1.0172, 1.0173, 1.0174, 1.0175, 1.0176, 1.0177, 1.0178, 1.0179, 1.0180, 1.0181, 1.0182, 1.0183, 1.0185, 1.0186, 1.0187, 1.0188, 1.0192, 1.0193, 1.0194, 1.0196, 1.0197, 1.0198, 1.0199, 1.0200, 1.0201, 1.0202, 1.0203, 1.0205, 1.0206, 1.0207, 1.0208, 1.0209, 1.0210, 1.0211, 1.0212, 1.0213, 1.0214, 1.0215, 1.0216, 1.0217, 1.0218, 1.0223, 1.0228, 1.0229, 1.0230, 1.0231, 1.0232, 1.0233, 1.0234, 1.0240, 1.0241, 1.0242, 1.0243, 1.0244, 1.0245, 1.0246, 1.0247, 1.0248, 1.0249, 1.0250, 1.0251, 1.0252, 1.0253, 1.0254, 1.0255, 1.0256, 1.0257, 1.0258, 1.0259, 1.0260, 1.0261, 1.0265, 1.0266, 1.0267, 1.0268, 1.0269, 1.0270, 1.0271, 1.0272, 1.0273, 1.0274, 1.0275, 1.0276, 1.0277, 1.0278, 1.0279, 1.0280, 1.0281, 1.0282, 1.0283, 1.0284, 1.0286, 1.0287, 1.0288, 1.0289, 1.0290, 1.0291, 1.0293, 1.0294, 1.0295, 1.0296, 1.0297, 1.0298, 1.0299, 1.0300, 1.0301, 1.0302, 1.0303, 1.0304, 1.0305, 1.0311, 1.0314, 1.0315, 1.0316, 1.0317, 1.0318, 1.0319, 1.0320, 1.0321, 1.0322, 1.0323, 1.0324, 1.0325, 1.0326, 1.0327, 1.0328, 1.0329, 1.0330, 2.0001, 2.0003, 2.0004, 2.0005, 2.0006, 2.0007, 2.0008, 2.0009, 2.0010, 2.0011, 2.0012, 2.0013, 2.0014, 2.0015, 2.0016, 2.0017, 2.0018, 2.0019, 2.0020, 2.0021, 2.0022, 2.0023, 2.0024, 2.0025, 2.0026, 2.0027, 2.0028, 2.0036, 2.0037, 2.0038, 2.0039, 2.0040, 2.0041, 2.0042, 2.0043, 2.0044, 2.0045, 2.0046, 2.0048, 2.0049, 2.0050, 2.0051, 2.0052, 2.0053, 2.0054, 2.0056, 2.0057, 2.0058, 2.0059, 2.0060, 2.0061, 2.0066, 2.0067, 2.0068, 2.0069, 2.0070, 2.0071, 2.0072, 2.0073, 2.0074, 2.0075, 2.0076, 2.0077, 2.0078, 2.0079, 2.0080, 2.0084, 2.0086, 2.0087, 2.0088, 2.0089, 2.0090, 2.0091, 2.0092, 2.0094, 2.0095, 2.0096, 2.0097, 2.0098, 2.0099, 2.0100, 2.0101, 2.0102, 2.0103, 2.0104, 2.0105, 2.0106, 2.0107, 2.0108, 2.0109, 2.0110, 2.0111, 2.0112, 2.0113, 2.0114, 2.0115, 2.0116, 2.0117, 2.0118, 2.0119, 2.0120, 2.0121, 2.0122, 2.0123, 2.0124, 2.0125, 2.0126, 2.0127, 2.0128, 2.0129, 2.0130, 2.0131, 2.0132, 2.0133, 2.0134, 2.0135, 2.0139, 2.0140, 2.0141, 2.0142, 2.0143, 2.0144, 2.0145, 2.0146, 2.0151, 2.0152, 2.0153, 2.0154, 2.0159, 2.0160, 2.0161, 2.0162, 2.0163, 2.0164, 2.0165, 2.0166, 2.0167, 2.0168, 2.0169, 2.0170, 2.0171, 2.0172, 2.0173, 2.0174, 2.0175, 2.0176, 2.0177, 2.0178, 2.0180, 2.0181, 2.0182, 2.0190, 2.0191, 2.0192, 2.0193, 2.0194, 2.0195, 2.0196, 2.0197, 2.0198, 2.0199, 2.0200, 2.0201, 2.0202, 2.0203, 2.0204, 2.0205, 2.0206, 2.0207, 2.0208, 2.0209, 2.0210, 2.0211, 2.0212, 2.0213, 2.0214, 2.0215, 2.0216, 2.0217, 2.0218, 2.0219, 2.0220, 2.0221, 2.0222, 2.0223, 2.0224, 2.0225, 2.0226, 2.0227, 2.0228, 2.0237, 2.0238, 2.0239, 2.0240, 2.0242, 2.0243, 2.0244, 2.0245, 2.0246, 2.0247, 2.0248, 2.0249, 2.0250, 2.0251, 2.0255, 2.0257, 2.0258, 2.0261, 2.0262, 2.0263, 2.0264, 2.0265, 2.0266, 2.0267, 2.0268, 2.0269, 2.0270, 2.0271, 2.0284, 2.0285, 2.0286, 2.0289, 2.0291, 2.0292, 3.0002, 3.0003, 3.0004, 3.0005, 3.0006, 3.0007, 3.0009, 3.0010, 3.0012, 3.0013, 3.0014, 3.0015, 3.0016, 3.0017, 3.0018, 3.0019, 3.0020, 3.0021, 3.0022, 3.0023, 3.0024, 3.0025, 3.0026, 3.0027, 3.0028, 3.0029, 3.0030, 3.0035, 3.0036, 3.0037, 3.0052, 3.0053, 3.0054, 3.0055, 3.0056, 3.0057, 3.0081, 3.0082, 3.0083, 3.0084, 3.0085, 3.0086, 3.0098, 3.0099, 3.0106, 3.0107, 3.0108, 3.0109, 3.0110, 3.0111, 3.0115, 3.0116, 3.0117, 3.0118, 3.0119, 3.0120, 3.0121, 3.0122, 3.0123, 3.0129, 3.0130, 3.0131, 3.0132, 3.0133, 3.0134, 3.0135, 3.0136, 3.0137, 3.0138, 3.0139, 3.0140, 3.0144, 3.0145, 3.0146, 3.0147, 3.0152, 3.0153, 3.0154, 3.0155, 3.0157, 4.0001, 4.0002, 4.0003, 4.0004, 4.0005, 4.0006, 4.0007, 4.0008, 4.0009, 4.0010, 4.0011, 4.0012, 4.0013, 4.0014, 4.0015, 4.0016, 4.0017, 4.0018, 4.0019, 4.0020, 4.0021, 4.0022, 4.0023, 4.0024, 4.0025, 4.0026, 4.0027, 4.0028, 4.0029, 4.0030, 4.0034, 4.0035, 4.0036, 4.0037, 4.0038, 4.0039, 4.0040, 4.0041, 4.0042, 4.0043, 4.0044, 4.0045, 4.0051, 4.0052, 4.0053, 4.0054, 4.0063, 4.0064, 4.0065, 4.0066, 4.0067, 4.0068, 4.0069, 4.0070, 4.0071, 4.0072, 4.0074, 4.0075, 4.0076, 4.0077, 4.0078, 4.0079, 4.0080, 4.0081, 4.0082, 4.0083, 4.0084, 4.0085, 4.0086, 4.0087, 4.0088, 4.0089, 4.0090, 4.0091, 4.0094, 4.0095, 4.0096, 4.0097, 5.0001, 5.0002, 5.0003, 5.0004, 5.0005, 5.0006, 5.0007, 5.0008, 5.0009, 5.0010, 5.0011, 5.0012, 5.0013, 5.0014, 5.0015, 5.0016, 5.0017, 5.0018, 5.0019, 5.0023, 5.0024, 5.0025, 5.0026, 5.0027, 5.0028, 5.0029, 5.0030, 5.0031, 5.0033, 5.0034, 5.0035, 5.0036, 5.0037, 5.0038, 5.0040, 5.0041, 5.0042, 5.0043, 5.0044, 5.0045, 5.0046, 5.0047, 5.0048, 5.0049, 5.0050, 5.0051, 5.0052, 6.0001, 6.0002, 6.0003, 6.0004, 6.0007, 6.0008, 6.0010, 6.0011, 6.0012, 6.0013, 7.0001, 7.0002, 7.0003, 7.0004, 7.0005, 7.0006, 7.0009, 7.0010, 7.0011, 7.0012, 7.0013, 7.0015, 7.0016, 7.0017, 7.0019, 7.0020, 7.0021, 7.0022, 7.0023, 7.0024, 7.0025, 7.0026, 7.0030, 7.0031, 7.0032, 7.0033, 7.0034, 7.0035, 7.0036, 7.0037, 7.0038, 7.0039, 7.0040, 7.0041, 7.0042, 7.0043, 7.0044, 7.0045, 7.0046, 7.0047, 7.0048, 7.0049, 7.0050, 7.0051, 7.0053, 7.0054, 7.0055, 7.0056, 7.0057, 7.0058, 7.0060, 8.0001, 9.0002, 9.0003, 9.0004, 9.0005, 9.0006, 9.0007, 9.0008, 9.0009, 9.0010, 9.0011, 9.0012, 9.0013, 9.0014, 9.0015, 9.0016, 9.0017, 9.0018, 9.0019, 9.0020, 9.0021, 9.0022, 9.0023, 9.0024, 9.0025, 9.0026, 9.0027, 9.0028, 9.0029, 9.0030, 9.0038, 9.0039, 9.0040, 9.0041, 9.0046, 9.0047, 9.0048, 9.0049, 9.0050, 9.0057, 9.0058, 9.0059, 9.0060, 9.0061, 9.0062, 9.0063, 9.0064, 9.0065, 9.0076, 9.0077, 9.0078, 9.0079, 9.0080, 9.0081, 9.0082, 9.0083, 9.0084, 9.0085, 9.0086, 9.0087, 9.0102, 9.0103, 9.0104, 9.0105, 9.0106, 9.0107, 9.0108, 9.0109, 9.0115, 9.0116, 9.0117, 9.0118, 9.0120, 9.0121, 10.0001, 10.0003, 10.0004, 10.0005, 10.0006, 10.0007, 10.0008, 10.0009, 10.0010, 10.0011, 10.0012, 10.0013, 10.0014, 10.0015, 10.0016, 10.0017, 10.0018, 10.0019, 10.0020, 10.0021, 10.0022, 10.0023, 10.0024, 10.0025, 10.0026, 10.0027, 10.0028, 10.0029, 10.0030, 10.0031, 10.0032, 10.0033, 10.0034, 10.0035, 10.0036, 10.0037, 10.0038, 10.0048, 10.0049, 10.0050, 10.0051, 10.0052, 10.0053, 10.0057, 10.0058, 10.0061, 10.0062, 10.0063, 10.0064, 10.0065, 10.0066, 10.0067, 10.0068, 10.0069, 10.0070, 10.0071, 10.0072, 10.0073, 10.0074, 10.0075, 10.0076, 10.0077, 10.0078, 10.0084, 10.0085, 10.0086, 10.0087, 12.0001, 17.0001.

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....Div. of Applied Research
2.0229.
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9.0110.
U.S. Veterans Admin.
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1.0072, 1.0073, 1.0161, 1.0162, 1.0219, 1.0224, 1.0235, 1.0262, 1.0312, 1.0313, 2.0002, 2.0029, 2.0030, 2.0031, 2.0032, 2.0033, 2.0055, 2.0062, 2.0093, 2.0136, 2.0147, 2.0155, 2.0156, 2.0157, 2.0183, 2.0230, 2.0231, 2.0232, 2.0233, 2.0234, 2.0235, 2.0241, 2.0252, 2.0253, 2.0254, 2.0256, 2.0272, 2.0273, 2.0274, 2.0275, 2.0276, 2.0277, 2.0278, 2.0279, 2.0280, 2.0281, 2.0282, 2.0283, 2.0287, 3.0031, 3.0058, 3.0059, 3.0088, 3.0089, 3.0100, 3.0101, 3.0113, 3.0114, 3.0124, 3.0141, 3.0142, 3.0143, 3.0148, 3.0149, 3.0150, 3.0151, 3.0158, 3.0162, 4.0031, 4.0055, 4.0062, 4.0098, 4.0099, 5.0039, 6.0014, 7.0027, 7.0052, 7.0059, 9.0031, 9.0032, 9.0033, 9.0042, 9.0051, 9.0066, 9.0067, 9.0068, 9.0069, 9.0070, 9.0089, 9.0090, 9.0091, 9.0092, 9.0093, 9.0094, 9.0095, 9.0096, 9.0097, 9.0098, 9.0119, 9.0122, 10.0043, 10.0054, 10.0059, 10.0060, 10.0079, 10.0080, 10.0081, 11.0003, 11.0004, 11.0015, 11.0016, 11.0017, 11.0018, 11.0019, 11.0025, 11.0026, 11.0027, 11.0029, 11.0031, 13.0004, 15.0004, 15.0009.
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2.0138, 2.0236, 3.0033, 5.0020, 10.0047.
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